BULLETIN

OF

THE JOHNS HOPKINS HOSPITAL

Entered as Second-Class Matter at the Baltimore, Maryland, Postoffice.

Vol. XXV.—No. 282.] BALTIMORE, AUGUST, 1914. [Price, 25 Cents

CONTENTS.

	PAGE
The Significance of the Thymus Gland in Graves' Disease. By William Stewart Halsted, M. D.	223
A Summary of Studies of Loco-Weed Disease of Sheep. By Harry T. Marshall, A. B., M. D.	234
The Behavior of Amœbic Dysentery in Lower Animals and its Bearing Upon the Interpretation of the Clinical Symptoms of the Disease in Man. By Walter Albert Baetjer, M. D., and Andrew Watson Sellards, M. D.	237
In Memoriam. Rupert Norton. By William S. Thayer, M. D.	242
Dr. Otto Gustaf Ramsay	243
Proceedings of Societies. Johns Hopkins Historical Club. Special Meeting, May 26, 1913, in Memory of Dr. John Shaw Billings.	244
Notes on New Books	253
The Quarter Centennial Anniversary of the Opening of The Johns Hopkins Hospital and the Twenty-first Anniversary of the Opening of The Medical School	254
The Herter Lectures for 1914	254

THE SIGNIFICANCE OF THE THYMUS GLAND IN GRAVES' DISEASE.

By William Stewart Halsted, M. D., Baltimore.

It was perhaps in 1849 that the first experimental proof was brought of the action which a ductless gland might exercise upon the organism. Berthold, professor in Göttingen, transplanted the testicles of young cocks and noted that the birds so treated developed the masculine voice, sexual desire, comb and love of combat. He thus in considerable measure anticipated Brown Sequard, to whom the doctrine of internal secretions is generally accredited and who twenty years after Berthold, committed himself to the view that a gland, whether possessed of ducts or not, elaborated substances which were essential to the growth and maintenance of the body and for the preservation of health. It was a memorable meeting of the Société de Biologie of Paris at which, two decades after his first pronouncement, this supergifted man related in support of his views the results of experiments made upon himself. He testified, as you recall, that following the injection of testicular juice he observed an astonishing revivification of his physical and mental powers.

One of the least understood and most complicated of the various distinct but intimately associated mechanisms at work in sustaining the orderly activity of the animal body is what has been termed the chemical correlation. Each organ, each tissue and each cell of the organism may exert a chemical influence upon some other far removed tissue of the body and thus aid in bringing about the adaptations and readjustments essential for the integrity and life of the whole.

The acid chyme passing into the duodenum stimulates the epithelial cells of the mucosa to the production of a substance which by way of the blood stream calls forth responses in pancreas, intestines and liver, exciting the secretion of pancreatic and intestinal juices and of bile. Bayliss and Starling proposed the name Hormones (ὁρμάω, to awaken, stir up) for such physiological products as serve to arouse the various organs to activity.

The structures which produce Hormones are commonly called endocrine (κρινεῖν, to separate) organs or glands of internal secretion.

Meltzer believes that, strictly speaking, such products of the chemical action of organs as must be regarded as terminal resultants of the decomposition processes, as the waste or by-products of metamorphosis, products which enter the circulation merely for the purpose of prompt elimination, should be differentiated from those substances which, formed in specific manner in individual or special organs, are taken up by the circulation and carried to distant parts, there to fulfil particular functions. Only these latter substances should, in the opinion of Meltzer, Gley and others properly be designated as Hormones, and Gley has proposed the appellation Parhormone for the decomposition products which invariably result from cellular activity and which as irritants might exercise a deleterious influence did not the fluids and tissues of the body form definite protective reactions.

Hormones can in two ways exercise their functions either by direct action upon the tissues or by means of the nervous system. In addition to these relatively direct methods of manifesting their action upon the terminal apparatus it is quite certain that the secretion of a given gland may act indirectly or through the agency of other hormonopoetic organs. For example, the influence of the thyroid by way of the thymus upon the activities of the stomach. To what extent the visceral nervous system plays a part and what may be the sequence of events in the course of the complicated interaction of the endocrine glands may in a measure be determined by experimental studies in metabolism. Thus it has been ascertained that in animals the glycosuria which develops on administration of adrenalin vanishes after excision of the thyroids. If these animals are now fed with thyroid extract the glycosuria reappears. On the other hand, in the pancreatectomized animals excision of the thyroid does not cause the glycosuria to disappear.

Studies in metabolism have taught us that the thyroid and pancreas on the one hand and the pancreas and chromofine system on the other reciprocally inhibit. Between the thyroid and chromofine system, however, there exists a reciprocal potentiation. Hence when hyperthyroidism gives rise to glycosuria it may conceivably do so by inhibiting the pancreas. In a still more roundabout way the thymus via thyroid, via pancreas might possibly bring about glycosuria unless, perhaps, the influence of the thymus upon the adrenals were protective.

Modern pharmacology regards as antagonists the sympathetic and autonomic* nervous system. As the sympathetic system possesses in adrenalin a specific pharmacological stimulant so analogously the autonomic system has in pilocarpin and muscarin its specific irritants. One can by the administration of thyroid extract produce symptoms in animals and man which strikingly resemble the stimulating effects of pilocarpin or muscarin (sweating, diarrhœa, disturbances in respiration, lymphocytosis, eosinophilia, etc.).

The standpoint has accordingly been taken that in the thyroid there is a constituent which produces an effect similar to that of the poisons of the pilocarpin group. In favor of this view speaks, especially, the well-known antagonism between thyroid extracts and atropin, which is an antidote for pilocarpin and muscarin. It has now been attempted on the basis of these physiological facts, which indicate that from the thyroid gland impulses may be sent out along the tracts of the sympathetic as well as the autonomic system, to distinguish the symptoms of Graves' disease which might be due to irritation of the sympathetic from those which might be attributed to autonomic stimulation. (Eppinger).

SYMPATHETICO-TONIC BASEDOW SYMPTOMS.

1. Pronounced protrusio bulbi.
2. Von Graefe, absent.
3. Löwi's phenomenon, positive.
4. Möbius, positive.
5. Dry bulbs.
6. Greatly increased activity of the heart with less pronounced subjective disturbances.
7. Sweating and diarrhœa, absent.
8. Falling out of hair.
9. Eosinophilia, absent.
10. Inclination to fever.
11. Alimentary glycosuria.
12. Refractory behavior to pilocarpin.

VAGO-TONIC SYMPTOMS.

1. Relatively moderate degree of tachycardia.
2. Pronounced subjective heart symptoms.
3. Von Graefe, definite.
4. Wide lid-clefts.
5. Möbius, absent.
6. Slight protrusio bulbi.
7. Increased lachrymation.
8. Profuse sweating.
9. Diarrhœa.
10. Disturbances of digestion.
11. Eosinophilia, likely.
12. Alimentary glycosuria, absent.
13. No adrenalin-glycosuria.
14. Pigmentation.

There are certain exceptional, more or less sharply differentiated cases of Graves' disease which every physician and surgeon who has actively interested himself in the subject must vividly recall. During the past twenty-three years in a series of about 500 I have seen perhaps twenty which were especially typical of their kind. The characteristic features which most of them presented were great emaciation, dilatation of the heart, sweating, diarrhœa, relatively slight exophthalmus, not excessive tachycardia, small goitre, and frequently a peculiar greyish bronze-hued skin.

Confronted with a case of this kind, I have repeatedly said to my assistants:

Here is another of these puzzling, dreadful cases. The patient is not highly thyrotoxic; the thyroid is hard, not large, nor pronouncedly vascular; if a lobectomy is performed she may die, but probably not with the stormy symptoms which suggest extreme thyroid intoxication. If death occurs it may be sudden, possibly not until several days after the operation, and perhaps when the patient seems to be convalescing.

In one of these cases death occurred four days after the ligation of a single artery under local anæsthesia. The operation, including the injection of the local anæsthetic and the sewing up of the tiny wound, required exactly ten minutes. One night, as I have said, four days after the operation, and a few minutes after the nurse had charted the pulse as 90, the patient awoke with a start, sat upright in bed, gasped for breath and died. The following case died suddenly about 30 hours after a thyroid lobectomy when we had ceased to be apprehensive about her:

CASE I.—A. V. C. (No. 33,010). Æt. 47. Admitted October 8, 1913. Except for whooping cough at the age of 15, mumps at 19 and measles at 21, patient states that she has enjoyed good health until about 4 years ago.

* This word is used in the restricted sense, and not as intended by Langley who proposed the term *autonomic* for the entire sympathetic system.

In January, 1909, patient experienced on swallowing the sensation of a "lump in her throat." At about the same time she was seized with a severe headache, became very nervous, suffered from palpitation and vomited several times. Thinks she had fever in this attack. Almost immediately the thyroid gland "began to swell." She was quite ill for 3 or 4 months but in May of the same year felt as well as ever. Her recovery was so complete that she considered herself in normal health until January, 1913, when she was taken ill again quite suddenly with precisely the same symptoms as in the previous attack. Palpitation and shortness of breath were more pronounced than at first; diarrhœa, vomiting and difficulty in swallowing also became troublesome symptoms. Cessation of the menses occurred about that time. Since July 1, 1913, she has been confined to bed.

Examination.—Patient is greatly emaciated (weight 67 lbs.); is very nervous, constantly jerking about and tossing her head; there is fine tremor of the fingers and tongue. She has decided mental aberration, ideas of persecution and grandeur; has bad dreams; talks to angels; is confident that her mind is affected, etc. Has staring expression; is very nervous; the whole body seems to be shaken by the heart-beat. The skin is ashy-bronze in hue. There is slight exophthalmus; definite von Graefe; convergence fair; rather wide palpebral clefts, but sclera covered. Joffroy sign absent; pupils react to light and accommodation. The hair is dry, grey, thin and falling out. Thyroid uniformly and moderately enlarged and very firm. Faint bruit but no thrill over thyroid arteries. No palpable enlargement of any lymphatic glands. The carotids throb forcibly. Veins of neck pulsate. There is great emaciation; deep supra- and subclavicular fossæ. Movements of respiration symmetrical. Lungs clear. Respiration 28. Thymus: there is no definite retro-manubrial dullness; X-ray negative. The heart is greatly dilated. There is a soft blowing systolic murmur over the whole cardiac area; it is heard best at apex. Pulse 140 to 155 and over per minute, and irregular. Arteries not hardened, blood pressure 115 to 125. Abdomen scaphoid. Marked aortic pulsation. Edge of liver not palpable.

Blood.—White corpuscles, 13,360; red, 4,404,000; hæmoglobin 61 per cent.

October 13, 1913. *Differential Blood Count.* 250 cells counted.

	Cells	Percentage	Actual number of each in cmm.
Polymorphonuclear neutrophiles	128	51.2	6840
Small mononuclears	86	34.4	4595
Large mononuclears	21	8.4	1222
Transitionals	5	2.0	267
Eosinophiles	3	1.2	160
Basophiles	1	.4	64
Unclassified	7	2.8	374
Myelocytes	2	.8	106

October 20, 1913. Patient vomited frequently until five days ago. Has two to three or more watery stools a day. Has persistent cough.

October 21, 1913. *Operation I. Ligation of Left Inferior Thyroid Artery.* The artery was easily found and tied. It was as large as a vertebral artery. Patient's pulse rose to 200 and over during the operation under novocain, nitrous oxide gas, and a few drops of ether.

October 24, 1913. Patient remarkably improved since the operation. Restlessness greatly relieved. Vomiting has ceased. Pulse now averages only 100.

October 25, 1913. *Operation II. Gas. Ligation of Right Inferior Thyroid Artery.* Artery very large, very thin-walled and blue like a vein. Operation required only a few minutes.

October 30, 1913. Patient has improved rapidly since second operation. Is quite cheerful. Hair regaining lustre.

October 30, 1913. *Differential Blood Count.* 250 cells counted. White blood cells 8300.

	Cells	Percentage	Actual number of each in cmm.
Polymorphonuclear neutrophiles	122	48.8	3984
Large mononuclears	37	14.8	121
Small mononuclears	69	27.6	2201
Transitionals	21	8.4	704
Eosinophiles	1	.4	41

November 4, 1913. Marked improvement in patient's general condition. Pulse 88. Patient eats heartily; neither vomiting nor nausea.

November 11, 1913. No pronounced change in patient's condition during the past week. Appetite large but there has been no gain in weight (60 lbs.).

November 16, 1913. Patient has gained 4¾ lbs. in past five days.

November 24, 1913. No definite improvement during past week.

November 25, 1913. *Operation III. Right Lobectomy.* Gas and a few drops of ether. Operation simple and rapid. Patient's pulse rose only occasionally to 180, but was usually about 160 during the operation. At the first operation it rose to 200 and over. At the end of the operation the patient's condition was excellent.

November 26, 1913. *Differential Blood Count.* 250 cells counted. White blood cells 18,400.

	Cells	Percentage	Actual number of each in cmm.
Polymorphonuclears	155	62.0	11,408.0
Small mononuclears	51	20.4	3,753.6
Large mononuclears	22	8.8	1,619.2
Transitionals	8	3.2	588.8
Eosinophiles	5	2.0	368.0
Basophiles	5	2.0	368.0
Unidentified	4	1.6	294.4

November 26, 1913. Patient had a fairly comfortable night and seemed to be convalescing satisfactorily until 1.20 p. m. to-day when she was found sitting up cyanotic and gasping for breath, coughing, trying to clear her throat, excited and apprehensive. Pulse very irregular. Respirations 40 to 50. Area of precordial dullness markedly increased, extending 4 cm. to the right and 10 cm. to the left of the median line. At 1.50 p. m. she became quiet, seemed fairly comfortable and dozed. Pulse 140 to 180 and irregular in force and rhythm. Cyanosis less.

3.40 p. m. Suddenly seized with another dyspnœic attack. Respirations became more labored and at 4.05 p. m. ceased. The heart apparently stopped beating about one minute before the cessation of respiration. The temperature rose to 101.5° F.

Autopsy. (Dr. Reid.) Subject strikingly emaciated. Left lobe of thyroid slightly enlarged; small slice of right lobe in region of the parathyroids. Cardiac dilatation. Emphysema of both lungs; broncho-pneumonia. Large thymus extending down to the auricles. Fatty degeneration and atrophy of liver; small adenoma of liver. Mesenteric glands rather larger than normal; otherwise no enlargement elsewhere of the lymphatic glands. Dilated, atrophic stomach. The thymus gland was thick but not broad enough to cast an X-ray shadow beyond the manubrium, It was triangular in shape, the finely tapered apex reaching to the top of the manubrium, the broad base extending to and partly covering the auricles of the heart.

The endocrine glands have been carefully studied microscopically and will probably be reported upon at other times by the various men to whom these organs were specially entrusted. I was particularly interested to find that in the thyroid glands the follicles instead of showing the usual picture found in exophthalmic goitre were for the most part circular and distended with densely staining colloid without vacuolation. The epithelial cells were low-cuboidal or flat. In places,

however, throughout the gland the colloid was rarefied and the cells high.

In this patient the vago-tonic symptoms predominated (diarrhœa, vomiting, small goitre, slight exophthalmus, definite von Graefe, Möbius* not pronounced, intense subjective symptoms, pigmentation).

Was this a case of thymus death?

Physiologists, pharmacologists, pathologists and clinicians are rapidly reflecting, consciously and unconsciously, helpful light for the interpretation of the clinical phenomena and dire results in cases belonging more or less definitely to this category.

In 1910 Meltzer* made the following cautious statement concerning the thymus gland:

With our present knowledge of the importance of the other ductless glands we are hardly justified in assuming that the thymus is a worthless fetal remnant. But we have to acknowledge that as yet there are no reliable observations or experiments which indicate clearly that the thymus has a function in post-uterine life.

Von Mikulicz (1895) called attention to the occurrence of enlarged thymus in severe cases of exophthalmic goitre, and Rehn (1899) suggested that it might be well to attack the thymus gland surgically in this disease. In 1908 Hart expressed the opinion that abnormal activity of the thymus gland might produce the clinical picture of Graves' disease.

It was my good fortune to be present when Garrè, at the 40th Congress of the Deutsche Gesellschaft für Chirurgie (1911) took part in the discusssion of Kocher's paper on exophthalmic goitre in order to report the first instance in which the thymus had been primarily removed for the cure of this disease. Although well aware of the fact that a "persistent" or revivified thymus had repeatedly been observed in "Basedow" he was astonished to learn from the statistics obtained by his assistant, Dr. Capelle, that a thymus persistens hyperplastica had been found in 95 per cent of the fatal cases, whether death was due simply to the severity of the disease, or occurred during the operation, or within twenty-four hours after the strumectomy.

So impressed was Garrè with these findings that he finally determined to test the effect of thymectomy in cases in which there was good reason to believe that the thymus was enlarged. It seemed to him that a severe and florid example of Basedow should be selected for the experiment and that the thyroid gland should be unmolested in the operation, the purpose of which was to determine the effect of a thymectomy upon the symptoms of the disease.

The result in his first case was as follows:

Clinically no definite influence on the struma, the exophthalmus or the eye symptoms, but an unequivocal improvement in the general condition as expressed by the "éclatant" quieting of the heart's action, rapid increase in weight, and a complete regression of the Kocher blood-picture, the lymphocytes falling from 40 to 25 and then to 10 per cent.

In his second case Garrè performed simultaneously a hemi-strumectomy and thymectomy.

The striking results which followed the first of these operations forced upon him the thought that the hyperplastic thymus in exophthalmic goitre displays an action essentially similar to that of the thyroid and that the thymus persistens aggravates the symptoms of the disease.

Professor Garrè gave to his assistant, Dr. Capelle, credit for the work and the thought which led them both to these conditions, which he said finds essential support in the proof by Klose that in the thymus-substance there is a heart-poison. Aside from the special action of the thymus there exist certainly, said Garrè, important reciprocal relations between these two glands, and for the following reasons:

1. After thymus extirpation, the blood-picture, which, by Kocher, is considered characteristic of Graves' disease, returned to normal precisely as after a successful strumectomy.

2. His assistant, Dr. Bayer, had recently demonstrated that intraperitoneal injections of the expressed juices of the thyroid as well as of the thymus produce the Kocher blood-picture, whereas the juices of colloid struma and of normal thymus influence the blood-picture to a much less extent.

3. They found in a thyroid gland which had been removed six months after a thymectomy microscopical evidence of regressive changes.

4. Gebele had announced at the previous Congress that the prompt implantation of normal thymus in thyroidectomized dogs prevented the appearance of cachexia strumipriva.

5. He was able to state, thanks to the permission of Dr. Bircher, that the latter had twice produced the typical Basedow picture by the intraperitoneal implantation of the fresh, pathologically hyperplastic thymus. These and other facts made him unable to subscribe to the generally accepted view of Möbius that the thyroid is alone responsible for the disease. On the other hand he was not prepared to take the extreme view of Hart that there was a purely thymogenic form of Basedow.

I have presented in such detail the views so briefly and cautiously expressed in 1911 by the highly gifted director of the surgical clinic in Bonn because this contribution of Garrè and Capelle marks an epoch in the developing story of Graves' disease and its treatment, the importance of which is as yet not realized.

During the past three years the research work on the thymus, which already had been considerable, has assumed great proportions, and for surgeons interested in Graves' disease this gland has become a theme on which their attention may well be focused.

And now, just a few weeks ago, appears a most convincing paper by von Haberer, the youngest of Billroth's assistants, and, until his promotion to the directorship of the Innsbruck surgical clinic, first assistant to von Eiselsberg in Vienna, who is also a distinguished product of the school of Billroth. The results of thymectomy in von Haberer's case, number 3, are so remarkable as to be almost unbelievable were they recounted by an authority less eminent and trustworthy.

* Meltzer. Animal Experimentation in Relation to Our Knowledge of Secretions, Especially Internal Secretions. Proc. of the Path. Soc. of Phila., Sept., 1910.

CASE 3.—Von Haberer.* Merchant, æt. 30; in his earlier years athletic; of late overworked in his business, but well until the autumn of 1909, when after an attack of fever, he noticed a marked increase in the frequency of his pulse, loss of zeal for work and a feeling of general bodily discomfort. About six months later he observed that his eyes were abnormally prominent, that he was becoming nervous and tremulous and subject to attacks of profuse sweating, and that he experienced feelings of cold in the legs. The greatly increased and irregular action of his heart caused him especial uneasiness. In the spring of 1911 a part of the thyroid gland was removed, and thereafter, for a time, his symptoms, the tachycardia excepted, were somewhat relieved. In the winter of 1911, after unusual business stress, the heart symptoms became greatly intensified and hæmoptysis and dyspnœa supervened. The dyspnœa became so great that the patient was apprehensive at times lest he choke to death. He sought relief at the hands of Prof. Kocher in Berne, who ligated the thyroid arteries of the unremoved lobe. No relief was obtained from the arterial ligation, on the contrary the patient's condition became alarmingly worse. He frequently had attacks in which a bloody froth was expectorated and consciousness lost. He finally could not walk without provoking these attacks.

On the seventh of December, 1912, the patient presented himself at the clinic in Innsbruck of von Haberer. He was cyanotic, gasping for breath and covered with cold sweat; the pulse could not be felt in the peripheral arteries. Fearing that the man might die in his office, Prof. von Haberer had him hastily despatched to a sanatorium. After a short rest in bed in a half sitting posture (the only one endurable for the patient) the pulse returned at the wrist. It was 160, very irregular and unequal. Exophthalmus was particularly pronounced on the right side; skin and mucous membranes cyanosed; slight von Graefe and Möbius signs on both sides; tremor and great dyspnœa; right lobe of thyroid very slightly enlarged; left lobe not palpable. Over both lungs signs of œdema and congestion-bronchitis; heart much enlarged, extending on the left side, four finger-breadths outside of the mammary line. Liver greatly increased in size, its lower thick border extending as low as the navel. Slight but definite icterus. Compression of the trachea by the thymus was excluded both by percussion and the Roentgen ray. There was, however, behind the manubrium a triangular shadow which, without demarcation, blended with the shadow of the heart. Percussion revealed no unusual dullness.

The patient begged piteously for operation, indifferent to its dangers; desirous only to be relieved of his great distress. Prof. von Haberer refused to interfere surgically, being convinced that if an operation were undertaken at that time it would result fatally. The physician called in consultation agreed that the patient's condition was hopeless, the heart being exhausted. The thyroid symptoms he regarded as a complication of relatively minor importance and believed that medication would accomplish nothing for the heart. The patient was kept in bed and treated with diuretin and digotoxin. In the course of ten days the condition of the lungs was somewhat improved, but the pulse, never dropping below 140, remained irregular with frequent periods of galloping rhythm. The differential blood count gave polynuclears 57 per cent; small lymphocytes 27.6 per cent; large lymphocytes, mononuclears and transitionals 12.3 per cent; eosinophiles 2.9 per cent; mast cells 0.2 per cent; coagulation was slightly delayed.

December 19, 1912. All were still agreed, and the patient assured, that he could not survive an operation of any sort. Nevertheless, von Haberer, having in mind the somewhat analogous case of Garrè's finally decided to yield to the patient's entreaties, and on December 19, under local anæsthesia, succeeded after prolonged search in extracting from behind the manubrium a piece of tissue 3 cm. long and ½ cm. thick, which resembled fat and macroscopically seemed to contain no thymus gland. Greatly disappointed at the result of the operation and believing that the last hope for the patient had vanished, von Haberer closed the wound. Towards evening of the same day the patient announced that he felt much better and that his dyspnœa had disappeared. On the fourth day after the operation he became much worse; the pulse was feebler and more frequent, the liver increased in size and the icterus deepened. The following morning, however, and each day thereafter improvement was noted, and on the third of January, 1913, two weeks after the operation, the patient was discharged from the hospital. Three months later (April, 1913) he returned for examination. The surgeons and physicians were astonished at the result. The apex beat was in the mammary line, the pulse 84, although still irregular, the cyanosis and icterus had disappeared; the liver was of normal size, and the color of the skin was good and fresh. The subjective condition was as satisfactory as the objective. The patient declared that he felt perfectly well; he could work as tirelessly as ever and could even climb mountains. In September of the same year this patient wrote that he had climbed for sport a mountain over 7500 feet high.

Three primary thymectomies have been reported, all of them from Garrè's clinic. To these may, however, be added Sauerbruch's case in which only the ligation of one superior thyroid artery preceded the operation on the thymus. In all of these cases the effect of the operation upon the general condition of the patient and upon the blood-picture was unequivocally beneficial. Of the combined operation, thyroidectomy plus thymectomy, eight cases have been reported by von Haberer; and Capelle and Bayer state that several times in the clinic of Garrè this operation has been performed.

Klose states in his recent book on the thymus gland that he has in five cases of Basedow's disease resected the thymus. In each instance there was striking improvement in the patient's general condition and return of the blood-picture to the normal. I have excised a small portion of the thymus with one lobe of the thyroid in two cases of which I shall speak later.

It has been our practice of late in the strumectomy operations to investigate the contents of the space between the trachea and the manubrium with the object of determining the possible presence of an enlarged thymus, and in a few instances we have made a fairly thorough search for this gland. Only twice have we found it enlarged; in both instances we should have been disappointed had there been no traces of thymus and our faith in some of the most important strands of the complicated web which the pharmacologists, the physiologists and the clinicians are weaving to represent the interdependent activities of the endocrine glands would have been shaken.

CASE 2.—H. P. (Sur. No. 31,648). Æt. 13. Admitted to the Hospital March 6, 1913.

Complains of difficulty in breathing, "feeling lazy," and inability to work. During the past four or five years he has had attacks of vertigo, occasionally with loss of consciousness; also attacks of nausea and vomiting preceded usually by headache. Patient might remain in bed for a week after such attacks.

Patient believes that his present illness began two years ago. He noticed first a swelling in the neck which has gradually in-

* Mitteilungen aus den Grenzgebieten der Med. u. Chir., Bd. XXVII, Heft 2, p. 210.

creased in size; then began to have shortnes of breath and the sensation of pressure on the trachea. He could not read aloud for any length of time. He could not run or ascend stairs quickly. During the past five months he has had dyspnœa on lying down and has been unable to sleep on less than three pillows. Ambition for work and play is lost. He is unable to talk loud and finds it impossible to shout. Has a hoarse cough and desire to clear the throat. For the past four or five months he has experienced some difficulty in the swallowing of solid foods, and at times even of liquids; his bowels are evacuated four or five times a day. He has occasional attacks of vomiting before breakfast. Has become irritable. Has not observed palpitation of the heart. Does not perspire excessively.

Physical Examination.—Boy is well nourished and well developed. The hair is oily; the skin neither abnormally dry nor abnormally moist. There is no exophthalmus; the von Graefe sign is positive at times; the other eye-signs are absent. The thyroid gland is enlarged to perhaps three or four times its normal size. There is definite retro-manubrial dullness. The X-ray shows a suggestive shadow. A soft systolic bruit is heard over a very slightly enlarged heart. The pulse is regular, 80 beats per minute. Tremor absent. Cervical, inguinal, submaxillary and axillary glands are palpable.

March 7, 1913. *Differential Blood Count.* 300 cells counted.

	Cells	Percentage
Polymorphonuclear neutrophiles	160	53.3
Small mononuclears	102	34.0
Large mononuclears	23	7.6
Transitionals	8	2.7
Eosinophiles	3	1.0
Basophiles	2	0.7
Unclassified	2	0.7

March 18, 1913. *Operation. Excision of Right Lobe and Isthmus of Thyroid and a Small Piece of Thymus.*

March 26, 1913. *Differential Blood Count.*

	Cells	Percentage
Polymorphonuclear neutrophiles	183	61.0
Small mononuclears	86	28.6
Large mononuclears	15	5.0
Transitionals	7	2.33
Eosinophiles	2	.6+
Basophiles	2	.6+
Unclassified	5	1.6

December 11, 1913. (9 months after operation.) *Differential Blood Count.*

	Per Cent
Polymorphonuclears	68.0
Small mononuclears	23.0
Large mononuclears	5.0
Transitionals	3.0
Eosinophiles	1.0

February, 1914. *Examination.* The boy's health is almost restored. He is able to do a full day's work but is rather more fatigued by it than are other boys of the same age. He can sleep on one pillow and has had no attacks of vertigo, nausea or vomiting since the operation. The cough and difficulty in swallowing have disappeared. The diarrhœa has ceased.

As the operation in this case was a combined one, the great improvement which followed it cannot definitely be attributed to resection of the gland alone. The portion of thymus resected was, however, so small that I am inclined to believe that the strumectomy rather than the thymectomy was chiefly responsible for the good result.

Case 3.—G. B. (No. 94,086). Æt. 12 years. Admitted to the hospital February 12, 1914.

Has had most of the infections diseases of childhood (whooping cough, measles, scarlet fever, chickenpox, mumps), all before she was 7 years old. Occasionally has sore throat but has never had a definite attack of tonsillitis. Function of eyes and ears normal. Has always been a nervous child with poor appetite. Digestion apparently good, although she has each year two or three "bilious attacks" with nausea and vomiting. For the past five years the mother has had difficulty in fitting the collars of her child's dresses, but not until a few months ago did she notice that the neck was enlarged. The eyes have always been prominent, protruding at times more than at others. For the past 3 or 4 years the child has complained of a feeling of fullness in the neck, especially when tired and nervous.

Examination. A rather pale, sallow-looking, frail girl. Expression alert and intelligent. She is unusually clever in conversation. Not obviously nervous at present. Hair normally lustrous. Hands and feet warm and rather moist. No pigmentation of skin. Dermatographia. No dilatation of superficial vessels of forehead or temples. Possibly slight fullness of veins of upper eyelids. Eyes decidedly prominent. Sclera well covered by lids. Palpebral clefts 1 cm. A suggestive stare. Von Graefe doubtful. No other eye-signs. Pupils react to light and accommodation. Slight tremor of tongue, none of fingers. Pulse regular; 100 beats per minute. Accentuated throbbing of the carotids, particularly of the right carotid. Dilatation of superficial veins of neck on both sides. Neck enlarged; rather more so on the right than on the left side. Both lobes of thyroid palpable, the right more definitely than the left. The isthmus is prominent and measures 2.5 cm. vertically. There is neither bruit nor thrill in the gland. Circumference of neck over the isthmus is 28 cm. The entire gland seems of normal or rather soft consistence. There is a suspicion of retro-manubrial dullness. The X-ray reveals, however, no shadow suggestive of the thymus gland.

Tonsils markedly enlarged; crypts visible. Posterior cervical and axillary glands are palpable. Finger tips are slightly clubbed. Child complains of palpitation of the heart and shortness of breath on exertion. States that on two or three occasions she has been obliged at night to sit upright in bed to relieve a feeling of slight suffocation. Has usually two and sometimes three stools a day. Has never been constipated.

February 12, 1914. *Differential Blood Count.* White blood cells 7000. Hæmoglobin 92 per cent.

	Cells	Percentage
Polymorphonuclear neutrophiles	120	60.0
Small mononuclears	71	35.5
Large mononuclears	5	2.5
Transitionals	3	1.5
Eosinophiles	1	.5

February 19, 1914. *Operation. Resected Right Lobe of Thyroid and a Small Piece of Thymus Gland.* The right lobe of the thyroid, about 2½ times the normal size, was resected according to our regular method, a portion of the posterior part being left to protect the parathyroids and the recurrent laryngeal nerve.

The thymus gland was found to extend upwards almost to the inferior pole of the right lobe of the thyroid. The piece of the thymus resected was hardly larger than the child's little finger.

February 21, 1914. (2 days after operation.) *Differential Blood Count.*

	Cells	Percentage
Polymorphonuclear neutrophiles	154	77.0
Small mononuclears	25	12.5
Large mononuclears	11	5.5
Transitionals	10	5.0

It is interesting to note the fall in mononucleosis. Nine days before the operation the percentage of mononuclears was 38; two days after the operation it had fallen to 18. The

child and mother are greatly pleased with the general improvement which they think has taken place since the operation. It is too soon for us to judge of this.

It is the belief of the few who have expressed an opinion on the subject that the overactivity of the thymus manifests itself chiefly or only after the hyperthyroidism has existed for some time—that it is not observed in the early stage of the disease.

In my patients 2 and 3 the thymus symptoms predominated (attacks of dyspnœa, diarrhœa, no tachycardia, not much enlargement of the thyroid and not very definite eye symptoms).

So one cannot but feel that the hyperthymusism may have been primary in these cases and that later on the thyroid symptoms might have predominated. We shall try to follow carefully the subsequent history of these children; and as only a part of one lobe of the thyroid and a very small portion of the thymus of each child was removed we may not have influenced profoundly the natural development of the disease.

A case upon which a double thyroid lobectomy was done two years ago returned recently for examination. The thymus being still enlarged it was treated for four hours by the emanations of 1300 milligrams of radium applied over 16 squares. Although there has been after 10 days no reduction in the size or density of the X-ray shadow, two thyroid nodules, as large as filberts, hypertrophied remnants of isthmus, entirely disappeared within 24 hours. Dr. Burnam, who applied the radium at Dr. Kelly's Sanatorium, believes that the thyroid nodules vanished because of the inhibited activity of the thymus. He thinks it is exceedingly unlikely that the emanations could have directly affected the thyroid.

The results of the combined operations have been, without exception, remarkably good; unmistakably better, I should say, than we ordinarily obtain from the operation upon the thyroid gland alone. Particularly striking has been the relative absence of the reaction which is usually observed in the 36 or 48 hours following thyroid lobectomy. The post-operative course in the experience of von Haberer could not be distinguished from that observed after operations for ordinary struma. This seems the more remarkable because in all these cases there was the complication of an enlarged and persistent thymus. The improvement was immediate and so strikingly pronounced that I agree with von Haberer in believing that it must be attributed to something more than mere accident.

That the thymus plays an important part in Graves' disease has, I think, been demonstrated beyond question by the results which have followed thymectomy. That some sort of relation exists between the two organs we have further evidence from the physical examination of the non-fatal cases, from the autopsy table, and from experiments on animals.

Palpation just above the manubrium, particularly pressure downwards towards the mediastinum, and over extension of the head, may be complained of by patients with persistent thymus on account of the shortness of breath occasioned by these maneuvers. The Roentgen-ray and the percussion-note over the area occupied by the thymus may give useful information; but the absence of both dullness and shadow does not exclude the presence of a persistent gland, nor do we know as yet how small a thymus may be responsible for symptoms.

It has been estimated as a result of non-operative clinical examination that in about 40 per cent of all cases of exophthalmic goitre the thymus is persistent. The actual percentage it remains possibly for the surgeon to determine by systematic exploration. We have, I think, no absolute evidence that the thymus may be completely wanting in a case of Graves' disease; and since, as I have stated, we do not know how small a fragment of this gland may suffice to play a part in the disease, we are not as yet in a position to assert that exophthalmic goitre may exist entirely uninfluenced by the thymus. Von Haberer, however, reports an outspoken case in which careful operative search failed to reveal its presence.

Enlarged thymus not infrequently accompanies colloid goitre. Attention was called by Astley Cooper and by Virchow to this association. The question naturally suggests itself, has the persistent thymus the same significance in both these forms of goitre, one of which we hold accountable for symptoms of hyperthyroidism, whereas with the other the picture of underactivity of the thyroid is associated? Is it not conceivable that the persistent thymus in colloid goitre may in some cases represent responses from time to time to periods of perhaps overlooked, hyperfunction of the thyroid, and if so that indeed for the "Kropfherz," a contributing factor may be found in the thymus?

From the post-mortem examination of cases of exophthalmic goitre which have died of intercurrent disease it has been ascertained that the thymus gland is persistent in about 82 per cent of them; and in those cases which have died of heart failure after operation enlargement has been found, as already stated, in about 95 per cent. Probably it will be ascertained that the percentage has been underestimated for the reason that enlargement of the thymus may not hitherto have been so completely noted or looked for as it will be in the future. Then, too, we must bear in mind the important lesson taught us from von Haberer's Case No. 3, that the severest thymotoxic symptoms may be caused by fragments of thymus so small as to be unrecognizable as such by the naked eye.

At the Johns Hopkins Hospital there has been only one opportunity to make an autopsy on a case of Graves' disease which died after operation. In this instance, as I have mentioned, a long, thick thymus gland was found tapering out from near the top of the manubrium sterni to the auricles of the heart.

What are the particular symptoms of Graves' disease which indicate a preponderate influence of the thymus? Eppinger, Garrè, von Haberer, Klose, Capelle, Bayer, van Noorden, Jr., and indeed almost every clinician who has familiarized himself with the literature would say it is the vago-tonic symptoms. But do we know quite definitely what the vago-tonic symptoms are? And in case they should be determined shall we be in a position to assert that the thymus is or is not alone responsible for them?

Naturally it will fall to the lot of the surgeon to discover which of the symptoms are dissipated by the removal of the

thymus; but even when this has been ascertained the proof is not furnished that no other organ could have had a part directly or indirectly in their causation.

Let us consider, for example, the protrusion of the eyeball, a symptom which according to MacCallum and others may be caused by stimulation of the sympathetic. If it is true that this is a sympathico-tonic symptom and if the thymus were activated solely by the autonomic system, the excision of this gland might not be expected to affect directly and promptly the exophthalmus. But as a matter of fact recession of the eyeball in at least one of von Haberer's cases was much more prompt than has perhaps ever been observed after strumectomy alone. The effect on the thyroid gland, particularly as to its vascularity, seems to have been quite as striking in von Haberer's experience; it must, however, be remembered that except in one case the combined operation was performed.

To discuss the grounds on which the various signs have been assigned to their special groups would carry us beyond the purpose of this paper. I might say, however, by way of illustration, a word with reference to the incomplete convergence of the eyes. This, the Möbius sign, is assigned to the sympathico-tonic group. It was explained by the late Dr. Landström and his supporters as due to the contraction of the Müller-Landström muscle of the orbit which is supposed to be responsible for the protrusion of the eyeball and by the particular arrangement of its fibers to embarrass the action of the internal rectus. There are some, and especially certain countrymen of Landström, who do not consider the demonstration complete that the Müller-Landström muscle is responsible for the exophthalmus. Furthermore, as I have said, the eyeball may promptly recede after thymectomy, and with its recession the Möbius sign may vanish, which is contrary to what might have been expected of a sympathico-tonic symptom after the excision of an organ activated chiefly by the autonomic or vago-sympathetic system.

Surgeons the world over have learned from an experience which is now very large that the majority of patients afflicted with exophthalmic goitre may be relieved of their symptoms by strumectomy, but that in a certain percentage of the cases the cure may be incomplete even after resection of the greater part of both lobes of the thyroid gland (Halsted).

I have performed perhaps 650 operations upon about 500 patients with Graves' disease. A one-sided lobectomy, the operation ordinarily done, has resulted in an approximate cure in possibly 60 per cent of my cases, but in at least 25 per cent the patient has not been sufficiently relieved by a one-sided lobectomy to resume her full duties, and in certainly more than 60 per cent (possibly 70 or 80 per cent) there remain symptoms of overactivity of the thyroid or thymus or of both of these glands sufficiently pronounced to be detected by the expert clinician.

The results of my experience as regards the cure of Graves' disease by one-sided lobectomy are quite at variance with the views of other surgeons.

In some 47 cases in which the improvement was altogether unsatisfactory after the excision of one lobe the other was removed. Of particular interest to me has been the observation, which we have made several times, that definite improvement may not be observed until both lobes have been almost completely excised. In a number of cases—all of them severe—in which the preliminary ligation of three or four arteries plus a single lobectomy was followed by little or perhaps inappreciable benefit the symptoms vanished, almost magically, on the removal of the remaining lobe. I should explain, parenthetically, that I never excise the entire lobe; a small slice is always left posteriorly to protect the parathyroid glands, for the reason that the chances are considerable that the other side may have to be operated upon. It is undoubtedly because surgeons have so universally confined their operations to the excision of one lobe plus, perhaps, the ligation of an artery of the other, that the results have not been better than they are. And you will agree with me that it is rather absurd to conclude that if the excision of an arbitrary amount of a gland supposed to be chiefly responsible for the symptoms did not cure or relieve them it would be useless to remove more of the offending organ.

Now although all of the symptoms including the exophthalmus may be cured by strumectomy, the blood-picture may remain unchanged, at least for a considerable period. We have, for example, five cases in our wards at present whose mononucleosis is as great and in one of them greater than before operation. In one the four arteries have been tied and one lobe resected. In two both lobes have been excised, and in the fourth, a very serious case, the inferior arteries were first ligated, then the superior arteries; next the right lobe and then the left was resected. This patient's health has already been almost completely restored but the mononucleosis is 53

RESULTS OF OPERATIONS FOR BASEDOW'S DISEASE.*

Year	Authors	No. of Cases	Cures %	Considerable Improvement %	Slight Improvement %	No Improvement %	Deaths %
1896	Schulz	20	90.0	....	....	5.0	5.0
1898	Wolf	9	....	66.5	....	....	22.5
	Helferich	6	66.6	16.7	....	....	....
1900	Reinbach (v. Mikulicz)	18	66.5	22.5	....	5.5	5.5
1902	Witmer (Krönlein)	23	40.9	36.2	9.2	9.2	9.2
	Th. Kocher	59	76.0	14.0	....	3.3	6.7
1903	Curtis	11	60.0	10.0	....	....	30.0
1904	Mayo	40	67.5	17.5	....	....	15.0
1905	Lessing (König)	8	50.2	....	37.3	....	12.5
	Hartley	21	87.5	....	....	....	12.5
1906	K. Schulze (Riedel)	50	72.0	12.0	....	2.0	14.0
	A. Kocher	167	93.7	....	....	....	6.3
1907	Itzina (Hildebrand)	7	85.7	....	....	14.3	....
	Mayo (only new cases)	136	78.2	19.6	....	....	2.2
	Landström	54	50.2	15.3	....	29.0	5.5
1908	Moses (Garrè)	28	16.9	41.6	24.9	12.5	4.1
	Klemm	32	93.2	....	3.4	3.4	....
	Th. Kocher	153	....	98.7	....	....	1.3
	MacCosh	22	14.5	72.7	8.2	4.6	4.6
1909	Hänel	21	38.1	42.8	....	....	....
1911	Sudeck	26	84.6	4.0	....	....	4.0
	Baruch	40	72.5	12.5	....	15.0	15.8
	v. Eiselsberg	44	61.4	34.1	....	4.0	....
	Enderlen	40	70.0	20.0	....	2.2	2.2
1912	Klose	61	75.5	9.8	....	1.6	13.1
	Weispfennig	30	60.0	6.6	....	23.3	10.0

*Klose, Die Basedowsche Krankheit. Erg. d. Inn. Med. u. Kinderheilk. Band X, 1913.

per cent (small mononuclears 34 per cent, large mononuclears 19 per cent), 4 per cent higher than on admission.*

Baruch, Sudeck, Klose, Melchoir, Lampé and Liesegang and others would seem to have brought proof from extensive clinical observations that the pathological blood changes in Basedow's disease remain uninfluenced by the excision of the thyroid gland.

Klose states it is universally conceded that all the symptoms of Graves' disease may disappear after thyroidectomy but that the disordered blood-picture is supposed to remain unchanged, and hence if we desire a hæmatological cure we must attack, surgically, the thymus. Another particular indication, according to Klose, for the excision or destruction of the thymus is the fact that in Graves' disease this gland is qualitatively and not merely quantitatively altered and may cause toxic as well as mechanical injury to the heart.

Borchardt a little more than a year ago reported † the result of his studies in the medical clinic of Lichtheim at Königsberg of the blood-picture in diseases of the endocrine glands. He examined 31 cases of Graves' disease, ten of status thymico-lymphaticus, five of simple goitre, fifteen of myxœdema (two of his own, and thirteen in the literature), thirteen of disease of the hypophysis (three of his own, ten in the literature), and five of Addison's disease (two of his own, three in the literature).

Borchardt found that in all diseases of the glands of internal secretion there was in the great majority of the cases an increase in the mononuclear cells, especially of the lymphocytes. There was leucopenia in about half of the cases, and approximately as often eosinophilia.

Since in all diseases of the thyroid, hypophysis and adrenals signs of status thymico-lymphaticus were established he concludes that the changes in the blood-picture are to be assigned to a status lymphaticus.

My observations do not permit me to accept in toto the views of Klose, Borchardt and the many others who attribute the lymphocytosis to the thymus. Of the 47 or more cases above referred to, operated upon during the past 20 years, in which I found it necessary to remove both lobes of the thyroid gland in order to relieve sufficiently the symptoms, about one-half have returned within the past two years for examination. In all of these, with perhaps two or three exceptions, the blood-picture is approximately normal. Of particular interest are the findings in a case at present in the hospital operated upon two years ago (double thyroid lobectomy). This patient was so ill when first admitted to the hospital, that I debated for some days as to the advisability of performing a lobectomy without the preliminary ligation of arteries. Her symptoms were predominantly vago-tonic but there were no signs of enlargement of the thymus. There was a mononucleosis of 53 per cent.

The improvement which followed the resection of one lobe being unsatisfactory the remaining lobe was excised. The blood-picture was at the time only slightly altered by these operations although there was marked improvement in her general condition.

Now, after two years, she was returned to the hospital for examination. She is almost restored to health and is able to perform all of her laborious household duties. She complains particularly of a sense of pressure behind the manubrium to which she attributes in a measure her shortness of breath at times. Percussion and the X-ray now indicate definitely an enlarged thymus. The blood-picture is, however, normal (mononucleosis 30 per cent).

Another patient (Miss. G. C.) has just come on for re-examination from Texas, in response to a telegram from me. A year ago when admitted to Dr. Barker's service in the hospital she was acutely and desperately ill and was promptly transferred to the surgical side. The thyroid arteries were ligated, two at a time, and then, one after the other, the thyroid lobes were resected. Vago-tonic and sympathico-tonic symptoms were about equally pronounced. There was extreme exophthalmus with all the eye-signs. Pulse 140-150; slight enlargement of the heart. Sweating, diarrhœa, nausea and vomiting, intestinal gas, bad dreams. Dyspnœa, vertigo and very severe muscular cramps. Mononucleosis 51 per cent. There was no evidence of thymus enlargement.

Now, after a year, she has gained greatly in weight, is, in fact, a little too fleshy. Her general health is fairly good and is gradually improving. But her condition is not satisfactory. Her pulse is 100-110, she suffers from dyspnœa on slight exertion, has very little energy and is greatly concerned about the exophthalmus which is still a conspicuous disfigurement.* The blood-picture is, however, normal (mononuclears 28 per cent).

From the facts gleaned at the autopsy table, from experiments on animals and above all from the results following primary thymectomies we have convincing evidence that the thymus gland may play an important part in Graves' disease, and in some cases assume the title role. Some of the most puzzling features of the disease are made possible of interpretation by the discovery of the influence which the thymus may exert.

That the secretions of the two organs concerned in the production of the Basedow picture have a relationship there can be little doubt. The injections and implantations in animals made by Svehle, Bircher, Bayer, Basch and Gebele demonstrate conclusively that the thymus and thyroid possess in common certain fundamental physiological properties.

Antagonistic factors are also at work in the two glands, the presence of which is indicated sometimes directly and sometimes indirectly by the behavior of other organs. There are

* These and many other cases controvert the opinion of von Lier who regards a lymphocytosis of 40 per cent as a contraindication to operation.

† Borchardt, Über das Blutbild bei Erkrankungen der Drüsen mit Innerer Secretion und seine Beziehungen zum Status thymico-lymphaticus. Deutsches Archiv f. klin. Med., Bd. 106, 1912.

* May 26. Within the past two months the patient's thymus has been treated with radium and the X-ray. The improvement has been quite marvelous. The exophthalmus has almost entirely disappeared and the patient considers herself almost well.

few in this audience * who are not familiar with the already famous experiments of Gudernatsch. To tadpoles equally developed, he fed to some the thymus of the calf, to others the thyroid of beeves. As a result of the thymus feeding the tadpoles increased greatly in size without differentiation or change in form. The creatures fed with thyroid promptly put forth arms and legs and otherwise rapidly took on the features of the frog. In the relation of the thymus and thyroid to the genital sphere and to the adrenals we find indications of a possible antagonism of some sort between the two glands. It is a well-attested fact that gravidity exercises a favorable influence upon the symptoms of Graves' disease. Basedow, himself, made this observation. This would seem to indicate that in pregnancy, in which unusual demands are made upon the thyroid, an excessive secretion from this gland can be utilized.

Between the thymus and ovaries there is experimental evidence of a possible functional antagonism. Thus Paton, Soli, Klose, Vogt and others have observed after thymectomy an increase in the weight of the ovaries, and according to Tandler and Gross there is abnormal persistence of the thymus in eunuchs.

Eppinger † relates of a case of Graves' disease of mild form in which immediately after castration toxic symptoms of threatening severity set in. He states that in the literature (reference not given) he has found a similar case. Of like significance probably is the fact that during the climacterium a mild may be converted into a severe form of Graves' disease.

Four or five years ago I was consulted in the North Carolina mountains by a native woman (Mrs. B.) who stated that for the previous six months she had been able to swallow nothing but liquids and for a week or more nothing but water. She was greatly emaciated and so weak that she could hardly stand. She was confident that the obstruction was just behind the "Adam's apple." The thyroid and cricoid cartilages were strikingly prominent, so much so that I confidently expected to feel a carcinomatous mass back of the larynx. I could feel nothing, however, except possibly an indefinite, soft mass of the presence of which I was not absolutely certain. She refused to come to the hospital, saying that she preferred to die at home. A year later I was surprised to find her robust and in perfect health. The difficulty in swallowing began to diminish soon after her visit to me, and in a month or two she was able to take food of all kinds as well as ever. The relief seemed to come quite promptly after the complete cessation of the menses. I concluded that a retrotracheal or retrocesophageal portion of thyroid had become enlarged during the climacterium.

As further evidence of an antagonism between the secretions of the ovaries and thymus we may mention the excessive lymphocytosis which has been observed by Klose to follow the injection of Basedow-thymus after oöphorectomy. Klose injected 5 cm. of thymus juice expressed from the gland of a Basedow patient into a spayed bitch whose lymphocytes after castration had risen to 32 per cent. Immediately after the injection there developed symptoms of severe Basedow intoxication. Shortly before death, which occurred one hour after the injection, the lymphocyte percentage was 64.

In one of my dogs (No. 9) which for 16 months had been deprived of both thyroid lobes and all the parathyroids except a graft, Dr. McCallum found complete absence of spermatogenesis. The testis as a whole was atrophic and spongy, but the interstitial cells of Leydig, although inconspicuous and perhaps somewhat degenerated, were still present in abundance.

What, then, is the relation of the thymus to the thyroid in Graves' disease? As stated by Capelle, the thymus can hardly be an "Erfolgsorgan" (a terminal apparatus), which enlarges simply in response to a stimulus from the specific gland. It is not merely antagonistic or compensatory (loose terms) to the thyroid, for if so its excision should be attended with an increase of the Basedow-symptoms. These organs, have, however, some sort of reciprocal relation. The effect of excision of the thyroid upon the thymus and of the latter upon the former organ has not been definitely determined.

In the dog (No. 9) just referred to, in which both of the thyroid lobes and all of the parathyroids had been excised, the thymus was carefully examined by Dr. McCallum, who at that time could have had no knowledge of its possible importance in Graves' disease. His report is as follows:

There is quite abundant thymus tissue. In the thymus there are some cysts, one of them quite large and lined by ciliated epithelium. Ciliated cavities of small size are found quite frequently through the tissue. I do not see any Hassall's bodies unless these might represent them. The thymus is not in the acme of its development, but has undergone a certain amount of atrophy.

Tatum found that the thymus of rabbits atrophied after excision of the thyroid.

As to the effect upon the thyroid of total excision of the thymus there is also uncertainty. The histological picture presented by the thyroid, seven months after total excision by Dr. McClure of my staff, and Dr. Park, Dr. Howland's assistant, of the thymus in a puppy, æt. 3 months, seems to be identical with that obtained by Matti and Klose, and interpreted by them as hyperplasia. On comparing the sections of the thyroids of Dr. McClure's dogs, of the control with that of the thymectomized animal, I should say that the changes in the latter indicate overactivity. These changes consist chiefly in entire disappearance of the colloid, and great increase in the height of the cells. The follicles are perhaps a little smaller in the hyperactive gland than in the control, and involutions are not conspicuous.

One can hardly be too cautious in assigning causes for the appearances found in one gland after excision of another, or in the remains of a gland after the resection of a part of the same. I am prompted to say this from experiences of my own, having particularly in mind our efforts to find the cause of the almost invariable hypertrophy of the thyroid in our dogs ex-

* This was delivered as a Harvey Lecture in New York early in 1914.

† Eppinger. Die Basedowsche Krankheit. Handbuch d. Neurologie, Bd. IV, Specielle Neurologie, III, p. 62.

perimented upon 26 years ago and to explain its absence after identically the same experiments during the past two years.

The pigmentation which has so emphatically arrested our attention in certain cases of Graves' disease deserves, I think, greater consideration than it has hitherto been accorded.

Our interest in this symptom has vastly increased now that we believe, I may say know, that the thymus may be an important factor in the disease.

As to the frequency of the occurrence of abnormal discoloration of the skin the statements of the various authors do not agree. Sattler, who gives the matter full consideration in his classical work on the symptomatology of Graves' disease, places it at 18 per cent. Kocher finds abnormal pigmentation of the skin once in 8 cases; Friedrich Müller observed it in 4 out of 5 of the serious cases. Murray noticed a more or less pronounced pigmentation of the skin 42 times in a series of 180 cases. There are some who think that this symptom rarely occurs. I have observed it chiefly in the instances of severe and of long-standing disease, and on reviewing the histories of my patients am impressed with the fact, as it seems to me, that the pigmentation has been more frequent in the vagotonic type of the disease.

This observation accords with what might be expected from animal experimentation and from the relation which has been observed by pathologists and clinicians of the thymus to the adrenals in status thymico-lymphaticus and in Addison's disease. Dr. Samuel J. Crowe of my staff, finds as a result of careful search of the records of the pathological department of the Johns Hopkins Hospital that in all the cases of status thymico-lymphaticus there is a note to the effect that the adrenals were atrophied, and that in Addison's disease hypertrophy of the thymus is almost invariably recorded.

Boignet and Calogero and Matzoukis found that excision of the adrenals was followed by hypertrophy of the thymus. Soli, Matti and, I think, Klose noted enlargement of the adrenals after thymectomy. Wastenson states that involution of the thymus may occur in consequence of the injection of the extract of the medulla and cortex of the adrenals. Possibly the extract of the medulla alone might have produced similar results, for Matti states that it is the medullary portion of the adrenals which hypertrophies in dogs deprived of the thymus gland.

Matti found, further, in his own laboratory an indirect confirmation of the above mentioned experimental data in that two animals with strikingly pronounced thymus-hyperplasia following extirpation of the spleen showed an extraordinary diminution in the amount of adrenal-medulla. In this constant reaction between the thymus and adrenal glands depressor influences are espied.

Treatment. Primary thymectomies uncomplicated by strumectomy, and secondary thymectomies in cases not sufficiently relieved by resection of both lobes of the thyroid would be the operations of choice for those searching for the essence of the Basedow thymus. The combined operation would be avoided by them as much as possible until it became more definitely known how profoundly and in what particulars the thymus may influence the disease. The excision of even a very small piece of either gland for microscopical examination, in the course of operation upon the other, might vitiate the experiment. For example, in our case 2 (boy æt. 13) the resection of a portion of thymus hardly larger than one's thumb was followed by almost complete relief of the symptoms, including a return of the blood-picture to normal—symptoms which would be considered thymo- rather than thyrotoxic.

We are debating what should be done in a case desperately ill in which there are reasons for believing that the thymus is enlarged. Should we first ligate the thyroid arteries at one or more operations or perform primarily a thymectomy? * The ligation of one and perhaps even of two arteries is less of a proceeding than the excision or resection of the thymus, but is it not possible that the removal of a part of the gland the more specifically responsible for the disease might be better withstood by the patient than an operation of less magnitude upon the other? In our Case I, for example, the ligations of the inferior thyroid arteries were followed by very little reaction and by great improvement in the general condition of the patient. Would it not have been better, we are asking ourselves, to have performed a thymectomy with her primarily in this case, or in preference to the thyroid lobectomy which was done subsequent to the ligations? The patient, you will recall, died suddenly one day after the strumectomy. These are questions to which further experience must give the answer.

I may say that except in the instance reported (Case I) we have had no death from a lobectomy which had been preceded by preliminary ligation of one or more of the thyroid arteries. And even in the case just cited I am inclined to think that death might not have occurred had I ligated the superior as well as the inferior vessels. I believe from my own experience that, disregarding for the moment the question of thymus resection, we have absolute proof of the advisability of ligating the thyroid arteries, as advised by Kocher, in the severest forms of Graves' disease, indeed in all cases where there seems to be the slightest ground for fear that the patient might not withstand the lobectomy. Most surgeons have abandoned or not practiced preliminary ligation of the arteries, contending that the repeated operations are more troublesome to the surgeon, are unpopular with the patient and yield no better results. As to the last point I am sure they are mistaken; as to the weight to be attached to the other two, each must be his own judge.

From the point of view of the research worker the combined operation, thyroidectomy plus thymectomy, should, as I have said, not be done, but when having excised one lobe of the thyroid I have found myself actually confronted at the operating table with an enlarged thymus I have felt compelled for the patient's sake to resect it.

There is much reason for hope that radium and the Roentgen-ray may give us the solution of this question. The blood of Basedow patients who have been treated with the X-ray

* May 26, 1914. For the past two months we have been treating the thymus gland of selected cases of Graves' disease with the X-ray. The results will be reported later.

shows remarkably little mononucleosis (Klose). Klose, Arella, Heincke, Peters and others have shown that under the influence of the X-ray the thymus rapidly undergoes involution, an involution which is so extensive that Klose expressly warns against radiation of the thymus region in children. The relative absence of lymphocytosis in Basedow patients whose goitres have been treated with the X-ray is attributed by Klose to the influence of the rays upon the thymus. In a case referred to earlier in the lecture it was mentioned that two nodules, remains of the thyroid isthmus vanished promptly after prolonged exposure of the thymus to 1300 mg. of radium. The gradual enlargement of these nodules had caused the patient great anxiety, and she was the first to notice that they had disappeared. Furthermore, she no longer experienced the feeling of oppression behind the sternum which had been a source of constant annoyance and occasionally of distress.

I have touched my subject only very lightly at some of the higher points. Hardly enough has been said even to make it clear that an enormous amount of work underlies the facts which we at present possess. It must be evident to everyone, however, that there reigns the greatest confusion on the subject of the function of the glands of internal secretion.

Fortunately the ardor for research on our globe is not diminished by the conviction that we are laboring in the wake of workers infinite in numbers on countless worlds who have carried their investigations millions of years beyond the stage reached by us, and are rapidly progressing towards an ultimate solution which may never be reached.

A SUMMARY OF STUDIES OF LOCO-WEED DISEASE OF SHEEP.[1]

By HARRY T. MARSHALL, A. B., M. D., Charlottesville, Va.

Eleven years ago, during the summer of 1903, I was engaged by the United States Department of Agriculture to investigate loco-weed disease in Montana, and I continued this study during the summer of 1904. The data thus obtained were worked up into two reports to the Department of Agriculture submitted in 1904 and in the spring of 1906. A more complete technical report was also submitted to the Department. The reports have not been published by the Department, and recently Secretary Houston has given me permisson to publish elsewhere. The full details of my studies will soon be published in the Bulletin of the Philosophical Society of the University of Virginia, Vol. I. In this article I shall give a brief review of my detailed report.

Widely spread over the western ranges from Canada to Mexico and from Kansas to California are many plants called loco-weeds. The plants properly called loco-weeds conform to two or three main types, all of which are members of the family Leguminosæ. These plants are hardy; bloom luxuriantly in the early summer and maintain themselves even where the soil is very poor, being most abundant, probably, in the higher plains and foothills east of the Rockies though not limited to this locality.

According to popular opinion, animals which feed upon these plants are attacked in the most remarkable way. They become crazy, hence the name "loco" or "crazy" disease; they are affected by the most peculiar mental and nervous symptoms; they become drug fiends, in that they want little else than the loco-weed to eat; they sooner or later emaciate and die from exhaustion or intercurrent disease. The length of the disease is not clearly described and many of the symptoms are extremely vague. Animals are supposed to teach one another the habit of eating loco-weed and often the disease will go through an entire herd or flock. The disease entered the United States from Mexico in the early stock-raising days of the west and gradually swept north and now it is found as far north as Montana. The losses resulting from it are supposed to be perfectly enormous, partly directly by death, but to a greater extent from the depreciation of the animals which are supposed rarely to recover.

Experimental studies upon the loco-weed and feeding experiments have given the most contradictory results, but it is safe to say that no one has succeeded in definitely identifying any poisonous principle, inherent in the loco-weed, and capable of producing the symptoms popularly associated with loco disease.

My studies were confined to the locoed sheep of Montana. Other locoed animals could not be obtained for study even after extended search for them. Most exhaustive inquiries were made of stock raisers concerning various aspects of the symptoms, the etiology and course of the disease. These inquiries alone served to show that stock raisers had not a single clear cut disease in mind in describing loco disease; the description of one stockman not tallying with that of another. It appeared probable from studying as a composite picture the information thus obtained that loco disease was something in the nature of an infectious process or at least that it was communicable, and that it attacked especially the younger and weaker animals and prevailed more particularly over ranges and feedings grounds which had been in use for ten or more years.

An important part of my work consisted in inspecting flocks of sheep suffering from loco disease and in examining in detail the most typical cases of severe loco selected from these flocks. Detailed autopsies were performed upon the selected animals after the symptoms had been studied as carefully as possible. The autopsy tissues were studied microscopically. It was hoped that these studies would establish postively the symptoms of loco-weed poisoning, and would reveal any anatomic changes resulting in animals which were victims of the locoweed.

It soon become evident that the "locoed" sheep from different flocks were not affected by the same disease. One flock, for example, presented emaciation and weakness as the chief

[1] Published by permission of the Secretary of Agriculture.

symptoms, and at autopsy these sheep were found to be heavily infected with a tapework of the liver, "*Thysanosoma actinioides.*"[1] A second group of sheep which were supposed to be typical locoes were overcome with bronchitis and respiratory distress. In these cases lung worms and pneumonias were very common. A third group of sheep whose behavior was regarded as most typical of locoed animals were found to be suffering from nasal and respiratory difficulties which were definitely proved to be associated with severe sheep fly infection (*Oestrus ovis*). A few other forms of parasite were encountered but the above mentioned were the most significant. In addition to these infections it became clear from inspection and from careful inquiry of the stock raisers themselves that the sheep in Montana, generally speaking, were insufficiently nourished. The ranges are grazed over so frequently that the grass does not have a chance to attain a good growth in the intervals between grazings; the flocks are too large for the available grazing grounds, while the grazing grounds are becoming curtailed as more and more open range is fenced in. Moreover in a large flock the delicate sheep have little chance to obtain good nourishment as they are crowded into the background by the stronger sheep.

A most careful study of the sheep failed to reveal anything in the least distinctive of the hypothetical loco poisoning either clinically or anatomically. The locoed sheep presented not a uniform picture as of a single disease, but varied appearances as from different diseases, any of which may be called loco disease by the ranchmen. The abnormalities observed in the selected specimens which I studied could be completely and satisfactorily accounted for by the evidence presented of underfeeding and parasitic infection. Moreover, a few very ill sheep, which were regarded by the ranchmen as typical examples of severe loco-weed disease, were kept under observation, and exhibited a distinct distaste for the loco-weed. At autopsy they were found to be emaciated, and to be infested with parasites. I therefore concluded that the animals which I had observed, although called locoed sheep by expert western ranchers, did not owe their condition to loco-weed poisoning, but were, in fact, examples of poorly nourished sheep, usually suffering from parasitic infection.

During 1904, in addition to continuing the examination of locoed sheep, an experiment was carried out of rather an elaborate nature in an attempt to produce pure loco disease in sheep by feeding them upon loco-weed. A tract of public land upon which the loco-weed, *Aragallus spicatus* (Hook.) Rydberg, was very abundant, and where no other poisonous plant could be found, was fenced in and divided into several lots. Eighty sheep—lambs, ewes and yearlings—were selected from a healthy looking flock and were dosed thoroughly with thymol and creosote in order to rid them of parasites. They were then divided into several groups and placed in a series of corrals. The sheep in some corrals were not allowed to eat loco-weed, but were fed abundantly with alfalfa hay. A second group were given only one-half rations of alfalfa hay, but no loco-weed. A third group were given no alfalfa hay, but plenty of loco-weed. A fourth group were given one-half rations of alfalfa hay and plenty of loco-weed. Another group were given plentiful rations of alfalfa hay and were also allowed to feed freely on loco-weed. The experiment was continued from July 15 to September 6, 1904, 54 days. The details of this experiment are recorded elsewhere. It will suffice to summarize the results here.

It appeared that the healthy sheep did not eat the loco-weed if they could easily obtain a plentiful supply of green forage, but it was easy to force them to adopt a loco-weed diet by reducing their food, or by reducing available green forage, even when the animal was given a plentiful supply of cut alfalfa hay. When once the animal had started to eat the loco-weed, in no instance did it appear to eat it to the exclusion of other food, although the animals may eat rather more of loco-weed than of any other single plant and may show rather a preference for it. In no instance did an animal eating the loco-weed exhibit any characteristic symptoms.

The animals which were not given alfalfa but were forced to feed on the loco-weed and the small amount of other forage in the corral suffered markedly from starvation. It was clear that this was no specific effect of the loco-weed because the animals receiving abundant alfalfa and also eating abundantly of loco-weed kept in much better condition and gained more in weight than those animals receiving only alfalfa and not eating loco-weed. In other words it appeared from this experiment that alfalfa and loco-weed is a better food for sheep than alfalfa alone and moreover it appeared that loco-weed alone does not keep the animal in a good state of nutrition.

Several other interesting points were indicated by this experiment. The sheep were divided into sets, some of which received salt regularly and others did not receive any salt during the course of the experiment. Strangely enough the animals which received salt gained less in weight than those which were unsalted, and among the animals which lost weight the unsalted lost less weight than the salted animals. The young animals were more severely affected by the insufficient diet than the adult sheep.

During the course of the experiment sheep fly disease (Myiosis), attacked all the corrals and was exceedingly severe in its effects upon the starved animals while the better nourished ones escaped with little damage, the sheep receiving alfalfa and loco-weed suffering less than any others.

The outcome of this experiment was to convince me that none of the abnormalities encountered in the sheep which I had studied could be attributed to the poisonous action of the loco-weed. None of my sheep gave the slightest evidence of having suffered any ill results from eating the weed. On the other hand the experiment seemed to confirm the view advanced in 1903 that the animals were suffering chiefly from starvation combined with one type or more of parasitic infection.

[1] The diseases produced in sheep by *Thysanosoma actinioides* formed the subject of a paper presented by me before the Association of American Pathologists and Bacteriologists in April, 1912, in which I described a new form of biliary hapatitis due to infection with this tapeworm.

My conclusions are at variance with the opinion held by members of the United States Department of Agriculture and further experiments have subsequently been conducted on the most elaborate scale by Crawford and Marsh. Crawford's work which led to the conclusion that the symptoms of loco disease are due to barium poisoning was soon upset by a publication by Alsberg and Black from the Department of Agriculture. Marsh's work is hitherto the last word from the Department on the subject of loco disease. I have gone most carefully and painstakingly over the available reports from Marsh and his colleagues and find that the several reports contain perplexing contradictions, and are lacking in important scientific details which it is necessary for Marsh to supply before his conclusions can be accepted. So far as I can make out from a careful study, Marsh claims that he has been able to produce with regularity, definite and fatal forms of poisoning in sheep, horses, and cattle by feeding them for a long time on loco-weed. Very few of his animals developed symptoms of locoism until they had been feeding on loco-weed longer than had my experimental sheep. He claims that there are definite and diagnostic symptoms which can be easily recognized when once they have been seen, and moreover—which is even more important, he claims that there are diagnostic anatomic changes in the animals which have died of loco poisoning. These anatomic changes consist essentially in ulceration and congestion of the stomach of horses or of the fourth stomach of sheep and cattle; of pronounced anemia; and of what are spoken of as serous collections around the heart and around the spinal canal outside of the dura mater. In the latter situation the so-called serous collections are frequently found in a state of organization. In addition there are frequently hemorrhages into the ventricles of the brain. In my more elaborate report I have analyzed carefully the writings of Marsh and have come to the conclusion that Marsh has by no means established the fact that the conditions he describes are due to loco-weed, and that up to the present time his work must be taken as a further substantiation of my claim that "loco disease" is not a clinical entity, because he has added one more to the list of diseases which go by the name of "loco-weed disease." Until Marsh gives definite and conclusive reports upon the nature of these remarkable spinal coagula and definitely excludes the possibilities of spinal meningitis and meningo-encephalitis, and until he fulfils other necessary requirements it cannot fairly be claimed that he has established loco-weed disease either as a clinical or as a pathologic entity.

The situation as it now stands is about this: The western ranchmen have for years been suffering heavy losses which have been attributed to the poisonous action of the loco-weed.

The Department of Agriculture, through Marsh's publications, has adopted the view that the ranchmen are correct in imputing their heavy losses to the loco-weed. Marsh urges the launching of a very expensive campaign against the loco-weed, with the object of eradicating it, a campaign for which I can find no reasonable justification.

My investigations have convinced me that there are several diseases of western livestock masquerading under the general name "loco disease." One hundred per cent of the severely "locoed" sheep which I studied were not suffering from locoism, but from underfeeding combined with parasitic infection. I therefore think there is reason to be doubtful as to the existence of pure, bona fide loco-weed poisoning, and I hold that it is perfectly certain that the heavy losses attributed to loco-weed disease, are at least in large measure due to other causes, which can usually be ascertained by careful study.

My investigations have brought to light several dangerous parasitic diseases of western live stock, and I have emphasized the fact that it is common for the animals to be distinctly underfed. My conclusions have received support during the last ten years through several publications from the Bureau of Animal Industry, dealing with various parasitic diseases of western live stock. A study of the literature upon the subject, and of the works of Marsh and Crawford, and a review of my own work leads me to believe that the very serious losses which occur among western live stock raisers demand attention, and that their interests can best be served, not by a blind assault upon the loco-weed, but by a vigorous campaign directed first at combatting the overstocking of ranches and the underfeeding of stock, and second at combatting the parasitic diseases prevalent over the western ranges.

NEW PUBLICATIONS.

The following six monographs:

Free Thrombi and Ball-Thrombi in the Heart. By J. H. HEWITT, M. D. 82 pages. Price, $1.00.

Benzol as a Leucotoxin. By LAURENCE SELLING, M. D. 60 pages. Price, $1.00.

Primary Carcinoma of the Liver. By M. C. WINTERNITZ, M. D. 42 pages. Price, 75 cents.

The Statistical Experience Data of the Johns Hopkins Hospital, Baltimore, Md., 1892-1911. By FREDERICK L. HOFFMAN, LL.D., F.S.S. 161 pages. Price, $2.00.

The Origin and Development of the Lymphatic System. By FLORENCE R. SABIN. 94 pages. Price, $2.00.

The Nuclei Tuberis Laterales and the So-called Ganglion Opticum Basale. By EDWARD F. MALONE, M. D. In press.

are now on sale by THE JOHNS HOPKINS PRESS, Baltimore. Other monographs will appear from time to time.

THE BEHAVIOR OF AMŒBIC DYSENTERY IN LOWER ANIMALS AND ITS BEARING UPON THE INTERPRETATION OF THE CLINICAL SYMPTOMS OF THE DISEASE IN MAN.

By WALTER ALBERT BAETJER, M. D.,
AND
ANDREW WATSON SELLARDS, M. D.

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OUTLINE.

I. Introduction.
II. Synopsis of the literature:
1. Spontaneous occurrence of amœbæ in lower animals.
2. Reproduction of certain clinical features of amœbiasis in lower animals:
a. Acute infections.
b. Liver abscess.
3. Failure to reproduce chronic infections with relapses or the carrier state in lower animals.
4. Appearance of symptoms, especially septicæmia, which are not described in man.
III. Behavior of typical strains of amœbæ in animals:
1. Material for study. Inoculation of six strains in forty-seven animals.
2. Reproduction of certain features occurring in human cases:
a. Acute fatal infections.
b. Chronic infections with relapses.
c. Carrier state.
d. Liver abscess.
3. Features in human cases which have not been produced in animals:
a. Intestinal amœbiasis with extensive lesions, but without dysentery.
b. Rarer complications of dysentery, such as brain and splenic abscess.
4. Features common in animals which have not been described in man: septicæmia:
a. Relation of septicæmia to therapy.
b. Relation of septicæmia to cause of death in amœbic infections.
IV. Behavior of atypical strains in animals:
1. Atypical features observed in man:
a. Continuous course of symptoms without intermission.
b. Absence of blood from stools.
c. Unusual morphology of the amœbæ.
2. Infection of ten animals with three atypical strains with reproduction of atypical features.
V. Comparison of gross pathology in man and animals:
1. Difference in distribution of the lesions.
2. Characteristic features of the acute and the chronic lesions.
3. Behavior of atypical strains.

INTRODUCTION.*

In the relationship between the infectious diseases of man and the lower animals many gradations, in regard to transmissibility, occur between the extremes of absolute immunity and pronounced susceptibility. In one group we find those diseases of man which the lower animals contract spontaneously with the reproduction of the typical clinical picture. At the other extreme we have those diseases of man to which all other species are not only naturally insusceptible, but to which they remain absolutely refractory, in spite of all predisposing factors that have been used to induce an infection. Conversely, it is even safe to assume that there are diseases which are absolutely specific for lower animals and which cannot be transmitted to man under any ordinary conditions. In this connection it has been found that experimental amœbic dysentery in lower animals runs a course which is strikingly similar, even in the finer details, to the rather complex course of the disease as it occurs spontaneously in man. Indeed, this similarity is so great that the study of the disease in lower animals is of direct value in the interpretation of the features that occur in man.

SYNOPSIS OF THE LITERATURE.

The spontaneous occurrence of amœbæ in lower animals is fairly common. The saprophytic amœbæ of the limax group occasionally pass mechanically through the intestinal tract when ingested with food. They are of no interest, however, except that they have occasionally been mistaken in cultures for the parasitic entamœbæ. They are not known to colonize in the intestinal tract in any animals, except possibly in certain marine fishes.[1]

The predominant types of amœbæ found in the lower animals are members of the obligately parasitic, but non-pathogenic, genus of entamœbæ. These occur in widely different groups such as the mammalia and amphibia. Occasionally one finds spontaneous infections in dogs and monkeys with pathogenic entamœbæ with the production of typical clinical symptoms, though the disease apparently does not occur epidemically or endemically among the lower animals.

Amœbic dysentery has been produced, in isolated instances, in a variety of lower animals, more especially in cats, dogs, and monkeys, but for extensive work, cats have been used almost universally. Some of the most important features of human amœbiasis that have been obtained in cats are (1) acutely fatal infections, and (2) the spontaneous occurrence of liver abscesses in infected animals. Certain prominent features, however, have not been observed in infected animals. Typical chronic infections have not been produced. It is hardly possible that the susceptibility of cats is so great that chronic lesions do not have time to develop, for many individuals are comparatively refractory. The experience of Craig[2] and Wenyon[3] may be taken as illustrating the usual behavior of infections in cats. In a comparatively large series of animals chronic infections did not develop. The longest

*For all of the inoculations directly into the lumen of the bowel, a laparotomy was done under general anæsthesia (ether). B. & S.

duration of the disease was four weeks and the remissions typical of the disease in man were not observed.

On the other hand, certain features have been observed in infected animals which have not been described in human cases though their occurrence in man is not improbable. Among the more important of these is the frequent occurrence of septicæmia in acute infections.

Clinical Course in Animals.—Observations were made upon the course of the disease in animals both upon the first transfer of various strains from patients to kittens, and also after the passage of a strain through a series of animals. This gave an opportunity to study the action of strains of varying degrees of virulence; and of strains the specificity of which for kittens had been modified to a variable degree by passage through a series of kittens. The following outline gives a summary of the material on which the observations in this paper are based:

ANIMAL INOCULATIONS.

Source of Strain	No. Inoculated	No. Infected	No. of Failures	No. Dying in Incubation Period	No. of Passage in Animals
North Carolina...	6	2	..	4	1
Panama City	3	2	1	..	1
Panama City	1	1	..	..	..
West Indies.....	6	3	3	..	3
Philippines	36*	27	4	5	11
North Carolina...	2	1	1	..	..
North Carolina...	3	2	1	..	..
North Carolina...	3	1	..	2	..
North Carolina...	1	1	..	..	..

* Four animals of this group were guinea-pigs. All the remaining animals in this table were cats or kittens.

In all, nine strains were inoculated successfully into animals. Of sixty-one animals inoculated, forty contracted an infection. Six of these strains were typical strains obtained from patients with symptoms of varying intensity. They were inoculated into cats and subinoculations were obtained with two of these strains. These patients had contracted their infections in widely separated regions: one came from the West Indies, one from the Philippines, two were from Panama City, and the remainder from the Southern States. All of these strains were transmitted successfully to cats. Forty-seven animals were inoculated, of which thirty-two developed definite clinical symptoms accompanied by the presence of active amœbæ in the intestinal discharges. The initial attack was sometimes preceded by a prodromal day of diarrhœa, though frequently at the onset formed stools were accompanied by bloody mucous discharges, the gross fæcal matter often being replaced soon by blood and mucus. In kittens the disease was uniformly fatal, most often in the first attack. In adult animals the initial attack was seldom fatal, the course being usually subacute or chronic and often ending in recovery. The animals which died acutely were of interest on account of the almost constant development of septicæmia and its bearing on the cause of death. The chronic cases were of interest from several standpoints. Some corresponded closely to chronic human cases, periods of apparent health alternating with acute relapses. In the interim between the attacks, the animals were free from symptoms, the stools were normal in gross appearance, and were frequently negative on microscopical examination; in such instances it was not possible to make a diagnosis of amœbic infection between attacks. In two adult cats a carrier state developed, the amœbæ persisting in one animal for three weeks, and in the other for two months without symptoms of dysentery. These two terminated in complete recovery. This carrier state developed only after an acute attack of dysentery had occurred; *i. e.*, there was no case in which animals were parasitized without producing clinical symptoms, though no specific attempts were made to obtain such a result. In a large number of human infections, Walker[8] found that individuals frequently became parasitized with *E. histolytica* and remained carriers over long periods, but without the development of symptoms. Clinically, such cases corresponded exactly in their behavior to cases of infection with *E. coli*.[8]

A few conditions have been described in man which have not been reproduced in animals. One of great importance, if substantiated, is the occurrence of intestinal amœbiasis, with the production of intestinal lesions, often sufficient to cause death, but without any symptoms of dysentery. Although such cases have been described in the literature, we feel that it would be extremely difficult to establish the authenticity of such a condition on evidence which is wholly free from objection. No evidence has been obtained in any of this experimental work in support of such a condition. In the infection in cats, dysentery was an early and prominent symptom. We obtained amœbic infections in guinea-pigs in which a secondary bacterial peritonitis developed without any symptoms of dysentery. This, however, is not comparable to the course of the fatal cases in man with extensive amœbic lesions, as described by Musgrave.[7]

The other conditions found in man which have not been reproduced in animals may be classified under the head of the rarer complications of dysentery depending upon secondary bacterial invasion. Examples of this are seen in the development of a brain abscess and of a splenic abscess. These conditions occur but rarely in man and their reproduction in animals would be of interest only from the standpoint of a curiosity. Indeed, in two guinea-pigs which we inoculated with *E. histolytica*, a peritonitis developed which proved fatal three days after inoculation. Examination of the stools of the animals at the time of inoculation showed no amœbæ. At the autopsy, *E. histolytica* was found at the site of the lesion in the bowel, which consisted in an area of inflammation without ulceration. The intestines were matted together around this lesion, and a bacterial peritonitis had developed which was becoming generalized. Two additional guinea-pigs were injected with a bloody mucous stool from a kitten. One of these remained well and the other died of a bacterial peritonitis ten days later. In addition to the localized inflammation of the bowel there was an area of definite ulceration and typical entamœbæ were found in the ulcer. However, there were no symptoms of dysentery, and no blood nor mucus appeared in the stools.

The infection of rodents is of interest in that they have not been used for the experimental study of amœbic dysentery and it is even reported that they are insusceptible to infection.[8] The advantage of using rodents would be obvious. However, we feel from this limited experience that although they are not resistant to pathogenic amœbæ, yet they are unsuitable for experimental work, both on account of their marked susceptibility to secondary bacterial invasion and also because they do not present typical symptoms of dysentery.

Liver Abscess.—In one case, an extensive liver abscess developed, occupying about one-quarter of the entire liver. This was found at autopsy in an animal dying six and a half weeks after inoculation. The initial dysentery had never cleared up completely and many motile amœbæ were found in the intestine at the time of death. Motile amœbæ were extremely abundant in the lesion in the liver. Stained smears showed no bacteria, but upon inoculation into nutrient media, a small micrococcus grew out in the majority of the tubes. This lesion, strictly speaking, was not an abscess, but consisted in extensive necrosis of the liver with beginning caseation. The important feature from a clinical standpoint, was that no fluid was present. Such a lesion would, of course, give the classical signs of liver abscess, yet upon exploration no fluid would be obtainable by aspiration and it might be impossible to confirm the diagnosis unless one were fortunate in securing a little necrotic tissue in the aspirating needle. The occurrence of extensive necrosis without abscess formation offers a ready explanation for the discrepancy which sometimes occurs between the physical signs and the findings at operation.

The one prominent feature of the animal infections which apparently has not been described in man is the frequent occurrence of septicæmia in the acute cases. In the case of the most virulent strain, septicæmia occurred in practically 100 per cent of all the young animals inoculated. In regard to human infections there is sufficient evidence to warrant the conclusion that septicæmia must occur at least occasionally. The bacterial invasions of the liver may, of course, be the result of an occasional embolus. In cases where a gangrenous bowel or a peritonitis develops, the probability of a terminal septicæmia is very great. The rare cases of brain or splenic abscess suggest very strongly that a septicæmia of longer or shorter duration was present. Finally, Strong has found that cultures of the heart blood taken post mortem, in cases of dysentery show the occurrence of secondary invasion by bacteria.[9] In connection with the significance of septicæmia, an instructive condition occurred in one animal. An acute, fatal attack of dysentery followed an injection by a high rectal tube. At autopsy, it was found that an extensive empyema had developed on the right side, and the pericardial sac was distended with yellow purulent fluid. Such a complication of a septicæmia suggests the existence of a general group of cases which give a history of typical amœbic dysentery accompanied by evidences of septic processes with suppuration in various parts of the body, as in the lung, the kidney, or other organs. The occurrence of septicæmia is of importance from two standpoints. In the first place, it was not possible to prove, experimentally, that amœbic infection of the intestine was capable of causing death by the primary action of the amœbæ. Indeed, the evidence pointed toward the contrary. Where death occurred it could always be explained by other factors; with one exception, death was due to secondary bacterial invasion. When such secondary invasion did not occur, the animals eventually recovered. If septicæmia occurs at all frequently in the acute fatal cases in man, it would have a very direct bearing, both upon the cause of death of such cases, and upon the explanation of the inefficiency of emetine therapy, which Rogers[10] has so frequently observed. The high leucocytosis (20,000 to 30,000) which is the rule in such cases is rather more suggestive of a bacterial than of a protozoan infection.

Behavior of the Atypical Strains of Dysentery.—Not only were the prominent features of dysentery reproduced for typical strains, but two distinctly atypical strains behaved in a remarkably similar atypical manner upon inoculation into animals. The following are the essential features of the most important case. A negro from the West Indies came to the hospital on account of a persistent diarrhœa which was sufficient to incapacitate him for work. He was passing eight to ten fluid stools per day, which were free from blood and practically free from mucus. The onset of the intestinal trouble occurred about ten years ago. In the early years of the disease, the stools were frequently bloody. In the past year the condition had been progressing slowly, there being no intermission in the symptoms, with periods of apparent health, such as are characteristic of amœbic infection. The general strength and health of the patient were good notwithstanding the intestinal trouble. Upon physical examination, a thickening of the sigmoid could be felt through the abdominal wall. Proctoscopic examination showed a thickening of the rectum, such as occurs in a syphilitic process. The Wassermann reaction was positive. Daily examination of the stool showed numerous flagellates, and after a saline purgation, one or two motile amœbæ were occasionally found. In specimens stained with hæmatoxylin, a few trophozoites were found after examining several slides. The nucleus of these was distinctly different from that of the usual pathogenic forms and the parasite could not be identified morphologically with any of the commoner types. Persistent attempts at cultivation, according to the usual technique, over a period of three weeks were uniformly negative. In addition to the 2 per cent of normal alkali which is usually added to the media, we employed varying percentages, from 0 to 2 per cent.[11] Conditions of cultivation were fully controlled. A culture of limax which had not been transplanted for more than two years, was found to be viable and grew well on all the media which were used in the attempt at cultivating these amœbæ from the human case. Upon inoculation of this culture of amœbæ into the rectum of two kittens, microscopic examination of the stools on subsequent days was uniformly negative. This strain of limax, however, was recovered by cultivation from the stool for a period of four days in both animals. In this respect the behavior of limax in kittens corresponds essentially to its behavior in man.

A still more crucial test was obtained, for we were able to cultivate a limax from the stool of a normal kitten which had not been previously inoculated with the organism. It was evident from these failures at cultivation that this strain of amœbæ, occurring in the diarrhœal stools of the patient, was not any ordinary strain of limax. Accordingly, an inoculation of stool was made at three sites; namely, into the cæcum, into the ileum one foot above the iliocæcal valve, and into the stomach. Six cubic centimeters were used for each injection. Microscopic examination of the material used for inoculation showed only one trophozoite, after the examination of several coverslip preparations. Cyst-like bodies were present containing two and often three nuclei.*

After an incubation period of one month a watery diarrhœa developed in this kitten, accompanied by fair numbers of amœbæ. This diarrhœa continued without intermission and without the presence of blood or any significant amount of mucus. The general health and nutrition of the animal not only remained good, but its growth continued rapidly without any interruption. The morphology of the amœbæ changed definitely, the nucleus becoming poorer in chromatin, but still remaining very much richer than in the case of *E. histolytica* or *E. coli*.†

After these symptoms had persisted for two months, the animal was sacrificed and two kittens were inoculated intracæcally. The incubation period in these two animals was shortened to five days and ten days, respectively; the injected material, however, was much richer in amœbæ than in the first transfer from the patient. In the second passage more mucus was present in the discharges and occasionally a few blood corpuscles were seen microscopically. Transfers were made from the animal with the longer incubation period to two kittens, one of which was inoculated by rectal tube and the other intracæcally. Only the second animal became infected, the incubation period being reduced to three days. No attempt was made to carry this strain further.

A second atypical strain was studied which corresponded very closely to the one just described. The patient, who had never been south of Maryland, had had a constant watery diarrhœa for eighteen months. Proctoscopic examination showed several ulcerated points in the rectum. A kitten about half-grown was inoculated intracæcally with the stool of this patient, and after an incubation period of one month, a watery diarrhœa developed, which persisted with practically no intermission for one and a half months. Numerous amœbæ were found in the discharges, especially after purging with magnesium sulphate. These were characterized by a chromatin-rich nucleus. After two months the symptoms had practically subsided. The animal was sacrificed; anatomically, the intestine was normal. No amœbæ were found in the mucosa.

In a third case, a boy of 14 years complained of a condition which anatomically was a giant colon. The stools had been constantly fluid for a period of eight years and frequently large blood clots were present. Microscopically, many flagellates and occasional amœbæ were seen. Morphologically, the trophozoites which were seen corresponded essentially to *E. histolytica*, except that there was somewhat more chromatin in the nucleus than one ordinarily sees. Injection into a kitten produced an acute bloody mucous diarrhœa of a few days' duration, which terminated promptly in recovery. Fresh specimens of stools were not obtained for examination and the amœbæ, which were seen, had evidently undergone degeneration.

Of the remaining strains which were studied, it may be said that the severity of the disease in the patient was a surprisingly good index of the virulence of the strain of amœbæ for kittens. Thus, chronic cases of long standing, with mild symptoms, often produced an attack in animals which was of comparatively short duration and eventually ended in recovery. Unfortunately, however, any strict comparison of the virulence of various strains for cats would be vitiated by the widely different ages of the animals which it was necessary to use.

The results with the atypical strains may be summarized as follows:

1. The incubation period was much longer than in the case of typical strains.

2. The clinical symptoms corresponded to those seen in the patient, the striking feature in some being the absence of blood from the stools and the continuous course of the symptoms without intermission.

3. The morphology of the amœbæ was atypical both in the patients and in the animals.

Comparison of Gross Pathology in Both Man and Animals.—The pathological lesions in the animals infected with typical strains of amœbæ corresponded in their essential features to the changes that take place in man. The acute and chronic stages were comparable to corresponding stages in human cases. The most prominent feature about the lesions in cats was their rather strict localization in the lower fourth of the large bowel. This was true regardless of the type of lesion which occurred. Even in the most acute cases the anatomical lesions were limited to the lower portion of the rectum, though in these cases where the fæcal contents were replaced by blood and mucus, numerous amœbæ were found throughout the lumen of the large intestine. Craig [l.c.] also reports that he found that the amœbic lesions in cats were most prominent in the rectum. No definite explanation suggested itself for this localization other than a remarkable specificity of the amœbæ. The most tangible difference that could be noticed between this portion and the middle or upper parts of the large bowel was the difference in consistency of the fæcal matter at the different levels, for it is only in the lowermost portions that formed fæces exist. The predominant location of the lesions in man is just the reverse of this distribution in cats. Rogers,[l.c.] in his experience of twelve years at Calcutta, found that the most frequent location was just below the ileocæcal valve. Only in a small percentage of cases were the lesions limited to the

* In a single instance, after the examination of several slides, a four nucleated cyst was found.

† A full description of the changes in morphology will be discussed in a separate communication.

rectum. However, in some instances, in which the lesions occurred higher in the bowel, there were scars of old lesions in the rectum and sigmoid.*

Description of Lesions.—The acute lesions which occurred for the most part in kittens, consisted in diffuse hyperæmia, congestion, and œdema of the mucosa and submucosa, giving rise to a granulomatous appearance. The serosa over such areas was usually bright from the injection of the vessels. Death took place before there was time for the development of any appreciable degree of ulceration.

In chronic cases multiple ulceration took place. In some instances healing occurred before the ulcers had advanced very far; in some of the fatal cases there was moderate undermining of the ulcers, but the extensive gangrene of the bowel, such as occurs in man, was not observed.

Pathological Lesions in Atypical Cases.—The pathological lesions in the atypical cases resembled the very mild lesions of the typical strains. Hyperæmia and congestion with swelling of the mucosa were well-marked features in some instances, though no ulceration was observed at any time. In the strain from the West Indies, the cat used for the first passage had practically healed at the time an anatomical examination was made and was essentially in the stage of a carrier. Of the two cats used in the second passage, the gross appearance of the large bowel in one was normal at autopsy; in the other it was slightly hyperæmic, and there were small areas of hæmorrhage. Of the two cats used for the third passage, the bowel in one was also normal, and the other showed changes only in the lower half of the rectum, the characteristic feature being a well-marked diffuse hyperæmia. The two animals used for the second and third atypical strains did not show any gross changes in the bowel.

Although the formation of ulcers with these atypical strains was not observed, nevertheless, we are not inclined to feel that it constitutes a point of absolute difference from the typical strains. It would seem probable that ulceration is only less common with the milder strains. In this short series of animals it might easily have failed to appear, for in the larger series with virulent strains it was observed in a perfectly typical form in only three instances.

SUMMARY.

1. The course of amœbic dysentery in cats corresponds very closely to the typical clinical picture which occurs in man. The acute and chronic forms of the disease, with the production of liver abscess and the carrier state, have been reproduced. No experimental evidence in cats was obtained which would suggest the occurrence of fatal intestinal amœbiasis without symptoms of dysentery. Rare curiosities, such as brain and splenic abscess, have also not been reported in animals.

2. Cases of intestinal amœbiasis which are remarkably atypical occur in man. Upon reinoculation of these strains into lower animals, infection takes place with the reproduction of the atypical features.

3. Extensive amœbic infection of the liver occurred in one animal with the involvement of about one-quarter of the liver substance, with extensive necrosis and caseation, but without the formation of any fluid. Such a lesion, occurring in the depths of the liver, would give all the typical clinical signs of liver abscess, but could not be diagnosed at exploration by aspiration unless liver tissue, obtained in the aspirating needle, were examined.

4. The acute and chronic types of lesions corresponded in the essential features of their pathology to human conditions. The localization of the lesions, however, was rather different from that seen in man.

5. Three of four guinea-pigs inoculated with pathogenic entamœbæ, contracted amœbic infection, but these animals proved unsuitable for study on account of the atypical course of the disease, and their susceptibility to secondary bacterial infection.

6. Bacterial septicæmia was a prominent factor in causing death in the infected animals. There are several features which suggest that it may play a more or less prominent part in the course of the acute cases occurring spontaneously in man.

7. No crucial evidence was obtained experimentally that *E. histolytica* is capable of causing a fatal infection in man in the typical course of the disease without the aid of secondary bacterial invasion.

* It is well to bear in mind the anatomy of the large bowel in the cat. It extends almost as a straight tube from the ileocæcal valve to the anus, lying practically in the mid-line.

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JOHNS HOPKINS HOSPITAL BULLETIN.

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IN MEMORIAM.

RUPERT NORTON.

1867-1914.

I knew him from the time he was seven years old. Shady Hill was the paradise of the boys and girls of Cambridge. In front of the old house so dear to generations of Harvard students who have received the kindly hospitality of his distinguished father—in front of the old house the land fell with a gentle inclination toward "Norton's Woods"; and this little slope, the nearest approach to a hill in the flatness of Cambridge, was known to us all as "Norton's Hill"—or "Norton's" for short. "Norton's"—what memories of delight that name brings! For there, on the winter days, within a few steps of the front door, all the boys and girls of Old Cambridge used to coast. No memory of my youth is more vivid. The welcome snow-storm; the laborious watering of the snow that the coast might be smooth and hard and icy; the rivalries with sled and "double-runner"; the unwelcome thaw. But above all, the glories of coasting by night; the beauty of the crisp, cold moonlight on the snow; the torches; the big double-runners; the older boys and girls, to whom we looked up with such awe and admiration—and envy when we, poor youngsters, were whisked home at an early hour. It is long years ago as I write, but it is still very near in my happy dreams.

At the bottom of the hill began "Norton's Woods," of refreshing memory. I wonder how many acres they covered. Not so very many, I fancy; and to-day they are in great part gone. But the fine old trees, the cool and mysterious shades, the rustling of the birds, are as fresh and real to-day as they were forty years ago. And so is the old house, with its long and leafy avenue, and the kindly face of its master, and the charming family circle.

It is with these scenes and memories that I first associate Rupert Norton. His brother Eliot and I used to pore over our stamp collections in the spring and fall, and in the winter we shared a double-runner. In those days Rupert, barely three years younger than we, seemed a little boy. He was then, as always, quiet and modest and reserved. Brought up at home in an atmosphere of books and art and scholarship, he entered college in the sophomore year. His life at Harvard was uneventful, his acquaintances not especially numerous but well-chosen and devoted to him. At the end of his college course he had a severe illness, and it was not until a year after his graduation that he began the study of medicine in Germany. There again our paths crossed, for at this time I also was spending a year in the laboratories and hospitals of Berlin. Our work was different and we met only occasionally; but when I was taken ill with diphtheria, he was at my side in a minute and was kindness and consideration itself. Helpful, thoughtful, self-effacing, he paid me all those little attentions which throughout life he has so unostentatiously showered upon his friends, and for which they feel so deep a gratitude.

After a year in Germany he returned to the Harvard Medical School where he finished his course in 1892, taking his degree in 1893, as was customary then for those who accepted hospital positions. After some months' service in the Children's Hospital of Boston, he came to The Johns Hopkins Hospital as assistant resident physician in the spring of 1893. The staff was then small; undergraduate teaching had not yet begun. His associates were Hewetson, Smith, Ramsay, Billings, Oppenheimer, Carter, Blumer, Futcher, Atkinson. Careful, faithful, thorough in his work, rather diffident in manner, he was not quick in making acquaintances; but before he left the hospital he was dearly loved by all of his associates. For behind the shy, diffident, rather abrupt manner, were hidden most lovable and charming qualities of mind and heart: a keen perception; a nice sense of humor; a most companionable, lovable, loyal nature—kindly and generous, charitable to a fault, intolerant only of that which seemed to him soft, unmanly or indirect.

In April, 1895, he left the hospital and began the practice of medicine in Washington—practice which was not rapid in coming to him; for he was too shy, too retiring, too reserved, and his peculiar reticence and even dryness of manner were too often interpreted as coldness and lack of interest. But those patients who came to know him, and the colleagues who broke through the shell of shyness and reserve, found one of the warmest, most generous and kindly hearts that ever beat. No one who knew Norton failed to love him.

In the Spanish War he enlisted as an Acting Assistant Surgeon and served throughout the campaign, doing, in the main, pathological work in one of the large Southern camps.

After this, to the disappointment of many of his friends, he gave up his Washington practice to become medical director of the Parisian office of a large American life insurance company. In his new work he displayed the same care and thoroughness that had been characteristic of all his endeavours. While many of us felt that the routine of this position was hardly worthy of one of his talent, yet in a way the situation had its advantages. The broad literary and artistic opportunities of Paris appealed to him deeply, and his life was far from empty. Outside of his work and other interests, Norton sought for and found opportunities to encourage and help his deserving fellow-countrymen of the artistic colony. How wise and thoughtful and discriminating his generosity was, few will ever realize, for his charity was known only to himself.

In 1906, the company with which he was associated abandoned its offices in Paris and Norton returned to the United States as Acting Superintendent of The Johns Hopkins Hospital during Dr. Hurd's long vacation. This position he filled ably and efficiently; and, on Dr. Hurd's return, he was appointed Assistant Superintendent of the institution. Here he soon made himself felt, not only in his administrative

capacity, but as a valuable helpmate to Dr. Hurd in the literary work connected with the position. In recent years he had published several thoughtful communications on subjects pertaining to hospital management, and his opinion and advice were beginning to be more and more widely sought. On Dr. Hurd's retirement, the editorship of the BULLETIN and the *Hospital Reports* fell on him. His services in this capacity were invaluable. His patience, his conscientiousness, his literary ability, his unfailing good taste, were relied upon by all. We had looked forward longingly for the day when we might have a library worthy of the hospital, in which Norton might find his proper position as director of the literary functions of the institution. It will not be easy to find his successor.

And during this time he has grown into our hearts as few men could.

After long years of tried and devoted friendship, Norton was married but twelve months ago, to Miss Cæcelia Hendrickson, of Frederick. No union could have been happier or more complete. How pitiful was its brevity!

How little, sometimes, can we measure a man's work in the world by his contemporaneous fame or by the permanent monuments which bear his name. Norton was not widely known, and he published little; but he did a good work, and he leaves many friends to whose lives he has added something uplifting and enduring. Only now that he has gone, do we who knew him begin to realize how large were his generosity and his charity, and how deep had been his influence upon us. But no one who knew him well, failed to realize at all times the unusual quality of his friendship, a friendship which meant not only perfect loyalty and devotion but other responsibilities not easy to fulfil, to which he was ever true. He who was blessed with his friendship never failed to receive, when it was needed, the kindly and just and direct word of warning or criticism so hard to give but so wisely and simply and considerately offered. His friends' honour and reputation were as dear to him as his own. For these friends, and they were many, he has done a noble and a lasting work. His memory will forever rest in their hearts, and through their better lives his influence will long endure.

When we look back upon his career, we shall remember his simplicity, his modesty, his upright, uncompromising honesty of purpose and word and practice, his delicate charm of mind, his varied attainments and interests and abilities, his faithful work in many capacities; but above all we shall remember the rare beauty of his friendship.

WILLIAM S. THAYER.

DR. OTTO GUSTAF RAMSAY.

The Faculty of the Yale Medical School places on its records this minute concerning Dr. Otto Gustaf Ramsay, whose death took place on Friday, June 12, 1914.

Otto Gustaf Ramsay received the degree of Doctor of Medicine from the University of Virginia in 1890, at the age of twenty. During the latter part of 1890 and the early part of 1891 he spent some time in postgraduate work at the College of Physicians and Surgeons, New York. In the fall of 1891 he worked in the medical dispensary of The Johns Hopkins Hospital, and in the summer of 1892 served as resident at the Garrett Children's Hospital. In the fall of 1892 he entered The Johns Hopkins Hospital as an interne on Professor Osler's staff, and served in this capacity for eighteen months. He then received an appointment on the Gynecological staff under Professor Howard Kelly, but left in the fall of 1894 to take charge of Dr. Kelly's private hospital, which position he held for about a year. During 1895 and 1896 he spent a year in Germany, working with Ziegler in Freiburg and visiting the important clinics. From the fall of 1896 till 1898 he was on Dr. Kelly's staff again, part of the time as resident. He left the hospital in 1898, but continued his work with the department as Instructor in Gynecology. He came to Yale in 1900 as Professor of Obstetrics and Gynecology, which position he held until his death.

Otto Ramsay was a man of strong personal charm. He was by nature genial and sympathetic, and inspired in his colleagues, his students and his patients a real and lasting affection. His personality, his great natural ability and his broad training in his chosen field, all served to make him what he was: a successful teacher, a thorough practitioner, and a man whose sympathies were always enlisted in the cause of the best ideals of his profession. With all this, he was extremely modest and unassuming. In his early professional life he found time to contribute to the literature of his specialty; but in his later years he was so driven by the exactions of a large practice that he seldom wrote, a fact which he not infrequently mentioned with regret. Through all the strenuous years which marked the close of his career he still, however, retained his academic sympathies.

Those of us on the Faculty who were associated with him will always look back on his useful and honorable career with the feeling that it was indeed a pleasure and a profit to have been associated with such a man.

(Signed) W. H. CARMALT,
H. B. FERRIS,
GEORGE BLUMER,
Committee.

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PROCEEDINGS OF SOCIETIES.

JOHNS HOPKINS HISTORICAL CLUB.

Special Meeting, May 26, 1913, in Memory of Dr. John Shaw Billings.

The meeting was called to order by the president of the club, Dr. Henry Barton Jacobs, who spoke as follows: This meeting has been called as a special meeting of the Historical Club, so that we here may join with other parts of the country in paying tribute to one whose influence has been so pre-eminent in this institution. In the beginning, his voice and his influence were most material in forming this hospital, and so as a tribute to him, we have met this evening. Dr. Hurd will open the exercises.

Dr. Hurd: I have always regretted keenly that I did not make memoranda in order to preserve in detail many interesting reminiscences which Dr. Billings from time to time gave of his early life.

He once informed me that he came of New England stock and that his parents were pioneers at the West; he being born in Indiana. I have an impression that his family removed soon after to Ohio, and I know from many things which he said that his early life was one of hardship, privation and considerable struggle.

He worked his way through college and later gave many interesting details concerning the privations which he endured. On one occasion, owing to a change in text-books—when he found himself under the necessity of spending, what seemed to him, a large sum for new text-books, an expenditure which had not been foreseen—he debated whether he should sell his overcoat or his undercoat, and finally parted with the latter, and wore his overcoat instead. The arrangement proved a judicious one until the warm weather of summer came, when he experienced more or less inconvenience from the heavy garment, and its manifest lack of suitability to summer wear.

He also spoke of the extremely plain fare which he prepared himself, generally cornmeal mush and milk (oatmeal not being then in fashion), and what he called "papered" eggs. He used to describe with considerable humor the details of cooking an egg upon the top of the stove upon a sheet of paper. The egg, if carefully watched, could be relied upon to cook sufficiently before the paper burned through; if, however, the cook became absorbed in literary matters or his attention was diverted, there was always danger that the paper would burn through and the egg would be spoiled. He always claimed that he attained great success in thus cooking an egg, and learned to do it to perfection.

In an address which he delivered at a commencement at Miami University, Oxford, O., he gave interesting details of his college life. His education seems to have been largely acquired by himself, and was not due to any great advantages for study or to special scholarly surroundings. He learned to use books, and to acquire knowledge. I know little or nothing of his medical school education, or of his hospital experience, prior to entering the army, and must leave these matters to others. Others also will probably give details as to his army life and his work as a bibliographer and sanitarian.

I am asked to say something of his services to the Johns Hopkins Hospital in its plan and construction. I have always believed that his most eminent services to the public were associated with the plans, construction and organization of the Johns Hopkins Hospital. I have recently had occasion to look over the series of five essays prepared for the information of the trustees of the hospital at the suggestion of Dr. Billings, and afterwards edited by him. These essays were written by Dr. Norton Folsom, at that time superintendent of the Massachusetts General Hospital, and an able hospital planner; Dr. Jos. Jones, of New Orleans, who had much experience as a sanitarian, medical writer and active hospital manager upon the Confederate side during the late Civil War; Dr. Caspar Morris, a retired Quaker physician of Philadelphia, whose work had been largely in diseases of children; Dr. Stephen Smith, still living at the advanced age of ninety-one years, who had shown versatility in medicine and surgery, as well as in administrative work such as hospital planning, inspection, lunacy administration and the like, and finally Dr. Billings whose services had been secured by the trustees because they wished to preserve as far as possible the experience which had been derived from the construction and administration of the hospitals of the United States Army during the Civil War. Each of these gentlemen prepared plans for the future hospital, and accompanied his plans with a description or an essay upon some branch of hospital construction, organization, or management. It is evident from a study of the plans originally prepared by Dr. Billings, that while they were in all respects superior to the others, they were much modified before the buildings were constructed. He originally favored buildings of at least two stories in height, and spoke of elevators and other arrangements for convenient administration which were later esteemed extremely heretical. When I came to the Johns Hopkins Hospital I was informed by the president of the Board of Trustees that the subject of elevators had been settled for all time, and that under no circumstances would the advisability of putting elevators into any one of the buildings ever be considered. It is evident from comparing the plans which were finally adopted and the original plan which Dr. Billings prepared that there had been a progressive evolution in his mind of the present plan, due probably to the study of other plans and his journey to Europe to perfect him. He always had an open mind, and sought counsel from experts. He further had the rare faculty of acting upon the essential part of another person's plan, and was able to modify it and to make it a part of his own, to the mutual advantage of both.

In 1877 he accepted the position of medical adviser to the Building Committee of the Board of Trustees, which really signified an arrangement by which he and the president of the board, Mr. King, were to plan and build the hospital.

The wards were to be built on the single story pavilion plan. This decision undoubtedly came from his experience in the

army hospital largely due, it seemed to me, to the general impression at that time—which we now know to be erroneous—that much disease was caused by miasma and malaria, which had their origin in emanations from the ground; hence, in all his plans, he decided to leave the basement unoccupied by patients and arranged also that wherever there was any communication between the basement and the first story, such as by flues communicating with radiators in the basement, even when they conveyed hot air, a thick coat of asphalt should be spread beneath them so that the floor might be wholly impervious to any exhalations from the soil.

He also made every provision against infection and contagion. No elevators were permitted in the buildings because of the danger of communicating infection from one story to another.

He also insisted upon perfect ventilation, not only by natural currents of air introduced from without, but also arranged for the removal of impure air from apartments by means of exhaust fans, and high shafts, with accelerating coils. He had a great desire to make everything perfect and no building up to that time, or since, had more enlightened arrangements for fresh and pure air, or more perfect construction of apparatus for heating and ventilation.

In the light of our present knowledge of hospital construction, the plan of his buildings is open to certain criticisms. The whole structure was too much upon the line of the army hospital. It was deficient in modern facilities for nursing and in the modern laboratories for studying disease. The sink rooms, ward bath rooms, linen rooms, etc., were too small, and not arranged for the convenience of nurses. They seemed to contemplate the presence of the army orderly at every turn. There was also imperfect provision for housekeeping and store rooms and other conveniences, which housekeepers love to plan and sometimes to use. The operating rooms were also inadequate and not sufficiently studied in the light of the present demands of modern surgery. These were minor defects and were incident to the times and not to any oversight on his part. There is no question, but that his plans influenced hospitals in a way unparalled in the history of hospital construction and that he gave a tremendous impetus to better hospitals, by directing the attention of medical men, sanitarians and others to the absolute necessity of certain great essentials, viz.: more perfect ventilation, and heating and the prevention of contagion.

In my relations with Dr. Billings, which at one time were fairly intimate, although of late years I saw little of him, I was always impressed with certain characteristics which stand out prominently in my mind.

He selected those things which it was essential to do with unerring instinct, and did not waste his time over unessential matters. This was evidenced in all his writings. I do not think that he ever polished his sentences or modified his original draft of any paper to any great extent. He set down in plain English the ideas which came to his mind, and they were usually so well considered and so self-evident, as to commend themselves to all who read what he wrote.

He had great quickness of decision, and did not waste his time in making and unmaking plans, but planned quickly and readily and then dismissed the matter from his mind. I remember when I was associated with him in the Chicago Hospital Congress of 1893, he gave me the names of certain physicians from abroad who ought to be invited to contribute papers, and the subjects of their papers, sketched out hastily upon a blank piece of paper while he was making the journey from Washington to Baltimore. Every detail was carefully considered, and from that draft it was possible to send out the invitations and to arrange that portion of the program. I doubt whether he ever gave it any more consideration.

He had a rare knowledge of human nature, and a certain dry humor which gave him great influence when he presented his views upon any subject. He was broad-minded and liberal; kind-hearted to all people and interested in their welfare. His face invited confidence. I remember on one occasion he told me that he had recently been approached by an ignorant market woman with a letter in her hand which she was unable to read. She asked him to step aside into a secluded corner in order that he might read aloud a letter from a wayward son. He found upon reading it that her son was in prison and that his mother fearing such to be the case, had not ventured to show the letter to any of her friends or acquaintances in the market, but had waited for a person in whom she felt she might have confidence that he would preserve her secret. She had selected Dr. Billings to read it, although an absolute stranger, because she saw at a glance that he would be worthy of her confidence.

Dr. Billings had, however, a certain intolerance of fools and was impatient of them in a manner which sometimes interfered with the success of his wise plans. He was too busy to waste his time in useless talk or windy argument and hence sometimes spoke his mind dogmatically and too plainly for his own good. I have always believed that had it not been for influences which came from politicians and others whom he had wounded by such praiseworthy intolerance, he might have been surgeon-general of the army.

He had rare powers of continued labor and by dogged perseverance accomplished wonders. I have never known a man who did so much work with so little friction and who brought things to pass so satisfactorily. I remember when he was preparing the Index Catalogue, that while much of the skilled work was done by trained experts and much of the unskilled work was done by unskilled labor, which he had been able to secure, instruct and direct—the last revision of it came under his own eye, and he read the manuscript of the Index Catalogue, volume by volume, and so complete was his revision, that in one volume of nearly or quite 1000 pages, the cost of changes in page proof was a little more than thirteen dollars! Could there be any better testimony to the industry, accuracy and scholarly attainments of the man?

He was above all a true friend, interested and unselfish, a loving husband, a kind father and a good son.

His life was a most active and energetic one up to its very close; only a few days before his death, I had the satisfaction

of meeting him at dinner, and was impressed with the vigor of his mind and his broad sympathy with and interest in every branch of knowledge.

COLONEL MCCAW: I am somewhat at a disadvantage compared with the other speakers to-night, in that I never had the inestimable privilege of working with Dr. Billings, or of being intimately associated with him. I met him when I was a youngster in the army and looked up to him with all reverence as one of the great men of the medical corps. I also visited him at his house in Georgetown. I am glad to say that at one time he made an application for me to come to Washington to learn the business of the library and museum under his tutelage. I think it was his idea to get a number of the younger officers detailed in Washington in succession to learn something about the work of the museum and library, so that when he gave it up, there would be several from whom to choose his successor. Unfortunately, this plan was not carried out. The Secretary of War would not consent in my case to make the appointment, and so I missed a great chance of preparing myself for the position I now hold. In his later years, when Dr. Billings visited Washington, he always came to the library to see his old friends, he spoke to all of the clerks and went in for a chat with his old friend, Dr. Fletcher. He generally honored me also with a short visit. He was always sympathetic, always had valuable advice to give and maintained to the last his interest in the library.

Living as I do in the institution which he built and in the midst of that great garden of medical literature which he planted and tended, I am amazed more and more every day at its completeness, its great scope, its catholicity and at the fact that nothing whatever connected with the literature of medicine has been neglected. It is not only the works of the masters of medicine—the great men of the profession—that appear there, but every irregular, every quack who has in any way written on the subject of medicine is represented in the library of the surgeon-general's office. It was Dr. Billings' idea that nothing whatever connected with medicine should be neglected, but that *all* should be collected and catalogued.

Dr. Billings was preeminent in everything. I think there is no doubt that whatever career he had undertaken he would have succeeded in it. He undoubtedly had the making of a great soldier. He would have made a great general. He would have made a most able prime minister, and he would have had his own way. He would undoubtedly have made a great ruler, probably an easier position to fill.

When he entered the service at 24, he came to Washington and appeared before the examining board, the last candidate to present himself. The board thought it was over with its labors and had made up the merit roll of the candidates, when the order to examine Dr. Billings was issued. The members of the board very soon found out that he was going to pass, and they also found out very shortly that he probably should be ranked first on the merit roll. So much to his dismay, after he had finished, as he thought, the examination in all the subjects set, after a consultation among themselves, they returned to anatomy again and began all over. Their idea was that they wished to be perfectly fair to the man who had already been ranked first upon the list, and they put to Dr. Billings all the questions they had asked him, in addition to those he had already drawn. As the result, Billings came out first in his class. He said that at that time he had three things which were novelties to the physicians in Washington. He possessed a hypodermic syringe, a set of clinical thermometers and a Symes staff. The possession of this last, and the fact that he had some skill in using it, led Dr. Tripler to give him as one of his first tasks, a series of operations upon strictures in old soldiers in Washington, old men valuable to the government at that time, and who would otherwise have been discharged and their services lost.

Very soon after this, almost immediately after being commissioned, he was given charge of Clifton Hospital in Georgetown, where he had under him several contract surgeons and 60 sisters of charity. He received there about 750 wounded from the seven days fight before Richmond, both Union and Confederate. He did nearly all the surgery, as he was practically the only operator at this hospital. It was here he did the first exsection of the ankle joint. A perfect recovery took place.

From Clifton Hospital he went for a short time to Philadelphia and then joined a regiment in the Army of the Potomac in time to be present at the battle of Chancellorsville. At Chancellorsville he was made an operating surgeon in the division hospital. He had there the most difficult problem that can be given to a medical officer in the field—that is, the care of the wounded and their carriage to the rear in the case of an army which is itself falling back. He chose two cottages [one of them the Chancellor house] in succession for his hospital. He was driven from both by brisk shell fire and finally had to take to the woods with his wounded and treat them under improvised shelter. At that time operation on the field was looked upon as a necessity. Nowadays the problem would be to dress as quickly as possible with the early aid packages and evacuate the wounded to the rear and so get them out of the way. At that time, however, it was considered necessary to do a great amount of operating on the field. Dr. Billings seems to have been a most successful and very able operator. Indeed he managed, even at Chancellorsville, to do a number of major operations, including gunshot wounds of the skull with injuries to the brain.

His next appearance was in the Gettysburg campaign. At Gettysburg he had his hospital established in a large house and barn on Round Top. When he rode up to take possession of this building, he was saluted by a volley from the enemy nearby. He found that the place had just been deserted by the occupants, fires were still burning, bread was ready for baking and water was boiling. He took charge of the wounded there without loss of time. Round Top did not prove a wholesome place for a hospital. In a short time he was driven out by brisk fire, and had to improvise a hospital in the shelter of the woods. This time the army was not retreating and he remained in this hospital about three weeks. He reported that

his wounded at this place did remarkably well, and the reason given is characteristic. He said: "They are in the open air, they have plenty to eat, they are being washed by a clean, warm rain and we have no flaxseed." His scepticism regarding the soothing flaxseed poultice and its value in "drawing" pus from a wound was ahead of his times, and in this also he proved himself a "progressive."

After Gettysburg, he was ill for a week or two, and from sick leave reported for duty around New York, and was in several of the large hospitals there.

At Spottsylvania, he was attached to the medical director's office of the Army of the Potomac, to which he was sent for the purpose of gathering statistics and data concerning the medical operations of the Army of the Potomac. His reports as medical inspector were full of valuable suggestions, both as to medicine and surgery and as to military administraion.

He came to Washington in 1864 and was assigned to duty in the surgeon-general's office, and on that duty, in one position or another, remained until he retired in 1895. The first five or six years of his service must have been very arduous. It is simply unrecorded drudgery. There is no minute record kept of the duties of an officer in a war department bureau, but these years must have been the most arduous of his life and, no doubt, among the most instructive. At any rate, he learned the ins and outs of government business from the beginning. He became acquainted with the manners and customs of comptrollers and treasurers. He knew the ways of Congressional committees, and was forming himself for the leading position that he soon took. He had charge of the disbursements of the hospital division, a most important task. He had charge of everything connected with the department of contract surgeons, of whom there were a great many at that time. He had charge of the organization of the veteran soldiers, a duty which required much medical knowledge. Altogether his work was of great importance. While in the office, he came in charge, a duty which he assumed for himself I suppose, of what was fondly called the library of the surgeon-general's office. This library in 1864 consists of a couple of large bookcases, or sets of shelves, with perhaps 1000 books. I have a catalogue of those books, which I sometimes show, as an object lesson, to people visiting the library. It is a little, very little pamphlet, with some of the titles in pen and ink and only a few printed. Even at that time, I suppose if those books had been handed over to an old book dealer, they would have been at once put out on the pavement and marked, "Any book on this table for 10c."

It seems to have always been his desire to establish a library and to index it properly. In fact he states that "the establishment of an adequate library for American teachers and physicians, with a reasonably good index, so that these people could, instead of reading over the indices of thousands of volumes in different places, obtain what they wanted in one," was his fondest aspiration. How well he succeeded and how far he surpassed his original aspiration, everyone who now knows the library can tell. We still carry on the institution along the lines that Dr. Billings laid down. We have not modified very much the routine method in which the material is cared for, in which it is indexed and in which it is loaned all over the country. The foundation that he laid, we rest upon still, and we try to carry on the institution as he would have carried it on.

From the thousand volumes in 1864, the library has now grown to half a million and a little over. There have been indexed over a million and a quarter titles of books, pamphlets and articles in periodicals. Eight thousand different journals alone have been indexed in the library, of which we still subscribe to a current list of about 1400. The institution far from being a "reasonably good library for the use of American physicians," is known all over the world. Through its catalogue, it is used almost as much abroad as it is here, and there is hardly a college, a university or a learned society in the country that has not at one time or another come to us for assistance.

All the time he was building up this monumental institution he seems never to have lost an opportunity to take part in any question affecting public health and welfare that came before him, and in every one he seems to have been preeminent. He made for two censuses, the tenth and eleventh, valuable reports on the vital and mortality statistics of the United States; he took a prominent part in fighting the epidemic of yellow fever at Memphis; he took a prominent part in the construction of the Johns Hopkins Hospital; and three or four other hospitals are largely due to his interest and the experience he had in hospital construction. He wrote an excellent history of surgery—Dr. Garrison thinks it the best history of surgery in English, a valuable paper on alcoholism, a treatise on ventilation and heating and innumerable papers and addresses. From his writings could be culled a little book of extreme value, of wit and wisdom—the kind of wit that does not grow stale, the kind of wisdom that helps every man because it is practical common sense. A few of his sentences one cannot but remember. His instructions as to the best way of writing a medical article are more valuable to a young writer than the reading of many essays and treatises. They were: First, have something to say. Second, say it. Third, stop when you have said it. Fourth, get a good title. The nearest approach to this is to be found in the matchless advice given by Humpty Dumpty to Alice, when she was giving him the history of her life. She asked: "Where shall I begin?" He answered: "Begin at the beginning, go on to the end, and then stop."

One extract from his presidential address before the Philosophical Society of Washington, December 4, 1886, I will read, as it is in a different vein from the others:

> **The old creeds are quivering, shifting, changing like the colored flames on the surface of the Bessemer crucible. They are being analyzed, and accounted for, and toned down, and explained, until many are doubting whether there is any solid substratum beneath; but the instinct which gave those creeds their influence is unchanged. . . . . When we examine that wonderful series of wave marks which we call the spectrum, we find, as we go downwards, that the vibrations become slower, the dark bands wider, until at last we reach a point where there seems to be no more movement; the blackness is continuous, the ray seems dead. Yet**

within this year Langley has found that a very long way lower down the pulsations again appear, and form, as it were, another spectrum; they never really ceased, but only changed in rhythm, requiring new apparatus or new senses to appreciate them. And it may well be that our human life is only a kind of lower spectrum, and that, beyond and above the broad black band which we call death, there are other modes of impulses—another spectrum—which registers the ceaseless beats of waves from the great central fountain of force, the heart of the universe, in modes of existence of which we can only dream.

He has passed beyond that dark band himself and the world is darker for his loss.

Dr. Jacobs: Since Colonel McCaw began speaking, Dr. Garrison has come in. I am wondering if he may not supplement Colonel McCaw's remarks.

Dr. Garrison: I have very little to add, but I have a very interesting picture of Dr. Billings which I should like to show you. A boyhood chum of Dr. Billings' son once told me a very characteristic thing about the doctor. The two boys had a chemical laboratory in the Billings home, and one time during their experiments they had an explosion, almost blowing out the side of the house. They were somewhat alarmed, but when the doctor came in and heard of it, he said absolutely nothing. He went in to his dinner and the thing passed off without any disturbance at all.

He cared absolutely nothing about the foibles of people, their little peculiarities, so long as they were doing their duty. He was always exacting about work. He was exacting of himself and exacting of others, as people of stern character are. Once there were two young fellows wrestling in one of his office rooms at lunch time. Dr. Billings had occasion to go that way on business. He peeped in, saw that they were wrestling, and then simply shut the door and waited until they got through. He then went in as if nothing had happened.

My relations with him were entirely official. I was never at his house but once, and at that time after 9 p. m., I found him piled up with books at work, as Dr. McAllister has described in the British Medical Journal. In my relations with him, I always found him an absolutely fair-minded, generous and courteous gentleman. I never had any difficulty with him myself, and I don't think any of the men about him had. They were devoted to him and his work. I mention these things, because I have sometimes heard Dr. Billings referred to as hard. That was because he was exacting, but as I have said, he was more exacting of himself than of anyone else. He worked for the government all day long, and as I happen to know, very often nearly all night long.

Dr. Jacobs: Dr. Norton knew Dr. Billings and I think you would all be interested in some of the personal details which he can give us.

Dr. Norton: I wish that I had known Dr. Billings better than I did. My friendship with him began years ago when I first came to the hospital and made the acquaintance of his son, then an interne in the hospital, who has been my friend ever since. My esteem for Dr. Billings grew as I came to know him more intimately. The last time I saw him was a few weeks ago at a dinner given to him by Dr. Welch. He was always interesting, and at this dinner most interesting. I think it is strange, considering how able he was, that he was not more widely known to the profession at large in this country. His friends, of course, knew his large powers, but he had none of that United States reputation that some men of much less worth and ability have. He was a modest man, but rightly knew his own worth and let others learn it by observation of his character and deeds, for he never boasted. He was a man of large frame, vigorous and soldierly. Agreeable and pleasant when you met him, he was easy to get along with, like so many men who have had to make their own way, and rub up against others and against the roughnesses of life.

Dr. Hurd has said a good deal that I was going to say. If I had written my paper, it would seem exactly as though I had copied it.

Dr. Billings was a good judge of men, and he did not judge them easily. He wanted to get out of men something that was worth while, and so he did not have any patience with those who were triflers. I think this came from his having made his own way, which he had to do largely, since as a young man his means were very small. This usually makes men severer in their judgment of others. But with him, it was not unkindness. He never said unkind things of anybody. One felt perfect security and confidence in him if one went to him for help. He was the confidant of many older men than myself. His son John tells me he has found out since his father's death that many men, more or less his contemporaries, went to him and confided in him on all sorts of questions. This shows the nature of the man.

I thought, as Dr. Hurd has said, that he was a man of quick judgment, that he must have been, but again I have learned that such was not the case. When you went to him for advice and oftentimes got a prompt reply, and wondering at his quick reply, probably asked him how he had come to form his opinion, he would refer to something that might have occurred some weeks or months earlier, which showed he had been thinking of this thing for some time. So it was not any cocksureness on his part at all in forming his judgment, which was always sound. One might not always agree with him, but he always had good grounds for his opinions. At the same time a man so capable as he was must have learned to use his mind quickly and with readiness and be able to pass judgment without hesitation; and he could do that.

As Colonel McCaw has said, he would have been a power in anything he undertook. I have often wondered if he might not have put through the Panama Canal, which Colonel Gorgas has done. He picked out his assistants well, and they were devoted to him, because of his loyalty, his readiness to help and his justice. I know there was one old colored servant in the family, whom he had had for forty years, who was devoted to him heart and soul. It may be said this is a trait of the race, but it speaks well for the master. Dr. Billings was a quiet man; there was never any bluster about him. He went ahead and worked, as we say, like a Trojan. He was thinking constantly, but was able to lay aside his worries when he went

home and to spend the evening reading novels. He was a tremendous novel reader. I doubt if any reader in America has read as many novels as he did, although he only read them as a recreation. Newspapers he did not care for, simply glancing over them in the morning. He had a very remarkable memory, as a man able to organize must have. He could not have compiled such a library as he did in Washington without having an extraordinary memory. He was in a sense retiring. He never appeared a great deal in public, although he was glad to meet scientific men, but I don't think he cared much for ordinary society. He was simple in all his tastes, and there was no affectation about the man. He was just a fine, strong man. Anyone who met him, could not help but feel that he was talking to a man of unusual powers and strength of mind.

DR. JACOBS then introduced Dr. Halsted, who spoke as follows:

DR. HALSTED: It is merely as a friend of Dr. Billings that I shall speak to-night at this little gathering, realizing that I can add nothing to what has already been said in praise of his character and marvelous achievements. Recollections of my first introduction to Dr. Billings in 1887 are still vivid, for I realized that I was under inspection at the intimate little dinner which Dr. Welch had arranged for the three. During this and the following year Dr. Billings would occasionally step into my room at the pathological laboratory to say an encouraging word or to discuss some of the problems connected with the surgical department of the hospital and university.

In the organization of the dispensary, with which I was entrusted, I frequently sought his valuable aid. It was at his suggestion that the card index was introduced in the dispensary, where its value was so convincingly demonstrated that subsequently it was adopted in the hospital; and he found for us a trained man who remained a year to assist in inaugurating the system, which was new for hospitals.

In this hospital so admirably planned by him, no special provision for surgery was made by Dr. Billings. He enjoyed emphasizing this intentioned omission and making the comment that inasmuch as no two surgeons would be likely to have the same views as to what the ideal operating room and its accessories should be, it would have been a hopeless task to attempt to satisfy the then unselected director of the surgical department.

I shall never forget his words or his look as he said to me after I had been told of my appointment, "Now you have the ball at your feet, all you have to do is to kick it." I understood his friendly, almost fatherly smile to say, "I am not quite sure that I approve of you altogether, but you may count upon my support." Since then he gave me many proofs that I had not misinterpreted his kindly glance.

Soon after the opening of the hospital Dr. Billings became my patient within its walls. One day as I was removing a subcuticular stitch of silver from his wound he protested, saying that the pain was considerable and that hence the procedure could not be ideal. I replied that we were experimenting with a new form of suture and had not as yet determined the proper time for its removal. "Oh, very well," he said, "go ahead, I can stand a little pain in a good cause." Once or twice he invited me to his home in Georgetown. I would join him at the surgeon-general's library and find him stuffing his overcoat pockets with journals and clippings. These he would take home with him every night and index before going to bed. He explained that these were details in connection with the indexing of the catalogue that he felt should be attended to by himself, and added, "If others see that I give careful personal attention to these matters they will realize that it must be worth their while for them to do the same."

Since then when oppressed by the seeming magnitude of one of my little anthills of work I have recalled the advice of Dr. Billings: "Devote a small amount of time each day to it and the mountain will melt away with astonishing rapidity."

The last time I met Dr. Billings was a few months before his death. We were traveling from New York to Baltimore and dined together on the train. His mental vigor seemed undiminished and his interest as keen as of old in his plans for the future of the various institutions which were guided by his masterful and dominant hand.

Dr. Billings was too great a man to be fully appreciated in his time.

The monuments of work which he has left are records the value of which cannot be estimated by the many, possibly by none; and the debt which others owe him for stimulus and suggestion can never be summed up.

Dr. Thayer was then asked to speak.

DR. THAYER: I well remember the first time that I saw Dr. Billings. It must have been something over twenty-five years ago when he delivered a series of lectures on the history of medicine at the Harvard Medical School. A valued teacher had told us that Dr. Billings was one of the most distinguished figures in American medicine, and even then, as a second or third year medical student, I had an almost reverent admiration for him as the editor of the Index Catalogue, and the Index Medicus.

I remember his appearance at that time. His tall, dignified, commanding figure, his impressive, forceful manner, his evident mastery of his subject left with us an impression which few have forgotten.

And then I remember vividly the first time I had the pleasure of meeting him. A few years later, while visiting in Washington, a warm-hearted and kindly, but highly eccentric lady, the wife of a retired army officer, who had known Billings as a young army surgeon, I was invited by my hostess at a late hour one evening to pay him a call; and so we set forth for Georgetown. It must have been about ten o'clock at night when we arrived at the door. No lights were to be seen. Evidently all had gone to bed. Undaunted, however, my good hostess rang the door bell. There was no answer. She rang a second and then a third time. Finally, the window over the door was opened, and Dr. Billings appeared in his nightgown. "Dr. Billings," said my companion, after

announcing herself, "I am afraid you have gone to bed." "Oh, no," he replied, "not at all, I will come down in a minute." "But I am sure you have gone to bed," answered the good lady. "Not at all," said he. "If you will wait a minute, I will come down at once." But my companion insisted, and compromised in the end by introducing me from the doorstep, in a voice, which I fancy, must have been audible for two squares. It was an impressive introduction in which the names, character and achievements of my ancestors for several generations were carefully recounted. At the conclusion of the address, it was requested that Dr. Billings name an hour on the following morning at which I might present myself at his office in the library.

The next morning, a shamefaced and embarrassed youth appeared at the surgeon-general's library, where he was received by Dr. Billings with a simple, kindly courtesy which he has never forgotten.

In the early years of this hospital, Billings was a frequent and welcome visitor, and all were familiar with him at his home in the library, that great library which is the Mecca of all American physicians.

What a work it was that he did in the foundation of that collection and what an undertaking was the Index Catalogue! It is impossible to estimate the debt of American medicine, the debt of the whole world to this man.

It has been said, and I believe justly said, that one of the most characteristic features of the scientific work of the American medical student is the completeness of his bibliography, and the familiarity shown by the author with the literature of the world relating to his subject. And how many realize that this is, after all, due in great part to the circumstance that Dr. Billings in that great library which he has built, that library which is so freely open to all, has accumulated an unexcelled collection of the widely distributed medical literature, and in the Index Catalogue and in the Index Medicus has given us a ready means of reference to this vast storehouse.

Twenty years ago, one of my friends, while in Munich, called upon his old teacher, Professor von Pettenkofer. Entering his library and turning towards his bookshelves, the old professor, with a sweep of his hand towards the Index Catalogue said: "That is the greatest work in my collection." I recall another incident which illustrates that which the Index Catalogue means in all parts of the world. In 1893, while looking up some matters in the Bibliotheque de l'ecole medicine, I sent to the desk a slip calling for a number of the then new *Archives des sciences biologiques de St. Petersburg*. The attendant handed it to the librarian on duty without comment. I observed his proceedings from a distant corner of the room. He looked at the reference for a minute, seemed puzzled, then turned and took from the shelf the last volume of the Index Catalogue which contained the title of the first volume of the series. Unfamiliar with the journal, his first thought was to search for it in our Index Catalogue.

Such a work as the Index Catalogue could have been accomplished only by a man of immense capacity, of extraordinary power of organization. These qualities Dr. Billings had. Whatever he undertook, the perfect implement seemed to spring to his hand; wherever he went, as if by magic, the most efficient co-workers surrounded him so naturally, so simply, so inevitably, that one might almost have fancied that it was the work of the hand of chance. But those who knew him saw in this grave, strong man, the mind of a master.

Where shall we look to-day for such breadth of conception, such an activating spirit!

None should revere the memory of Billings more than we, for this hospital is his child, and few realize what we owe to his wise counsel in the days of its infancy. We, the guardians and the offspring of this child of his, must see to it that his name is perpetuated among the buildings which he designed, by a memorial worthy of the man. Here, of all spots, there ought to stand a dignified edifice which should bear the name, "The Billings Memorial Museum and Library," which should gather together the scientific collections and the books from the hospital and the medical school, which should offer here, near the greater foundation in Washington, ample opportunity for the study of the history of that art to the service of which this great man so nobly devoted the major part of his life. Such an institute would be a fitting honor to a noble memory.

But, alas, it can never give to those who follow us the memory of the man which is ours—the dignity of his presence, the firmness and gravity of his speech, that rare sense of poise and balance and power which he impressed upon all who approached him. It was good to have seen and to have felt all this. Something, to be sure, is preserved in the beautiful portrait by Cecilia Beaux, but it is a sadly small part of what we who have known him could wish to transmit to those who shall follow us.

Dr. Winford Smith, the superintendent of the Johns Hopkins Hospital, was next introduced.

DR. SMITH: I cannot speak of Dr. Billings as one who was privileged to know him personally. It has been my regret that I was not so favored. Of Dr. Billings as a student, a scholar, a physician, and an organizer, others have spoken.

Dr. Billings was so long associated with this institution, he did so much for it, his judgment was so sound and the principles which he helped to establish have had such far-reaching influence, that I wish to recall on this occasion certain thoughts of his as expressed in his address on the occasion of the opening of the Johns Hopkins Hospital, nearly a quarter century ago. Dr. Billings said:

The third principle to be kept in view, in such a hospital as this, is that it should provide the means of giving medical instruction; for the sake of the sick in the institution as well as out of it. It is well known, to those familiar with the subject, that the sick in a hospital where medical instruction is given receive more constant, careful and thoughtful attention than do those in a hospital where no such instruction is given. The clinical teacher must do his best; keen eyes will note every error in diagnosis, every failure in results of treatment. Moreover, the very act of teaching clarifies and crystallizes his knowledge; in attempting to explain, the dark places become prominent and demand investigation: and hence it is that those cases which are lectured on receive the best treatment. I need say nothing here

on the other side of the question, the value of properly trained physicians to the community and the necessity for hospital instruction in such training. . . . .

Closely connected with this subject of teaching is that of increasing our knowledge of the causes, symptoms, results and treatment of disease, in fact one cannot be thoroughly well done without the other, and hence many of the provisions for the one are also useful for the other. . . . .

One structure is very largely devoted to and fitted for experimental research, and that is the pathological laboratory, where the causes, processes and the results of disease are to be studied. Upon the results obtained in that laboratory may yet depend the saving of many lives; the relief of unspeakable agony, the warding off of pestilence from the city, and, to put it in a strictly business light, the value of real estate and the rate of taxation of this community. We are on the verge of great advances in our knowledge of the causes and methods of disease, and I feel sure that these will be only preliminary steps to far greater and better knowledge of how to prevent them or to treat them than we now have. The probable length of life of the new-born infant to-day is not much more than half what it ought to be, the practical productive period of life of our men and women is shortened and interrupted by unnecessary disease and suffering; but remember, if these things are to be amended it is not merely by teaching old doctrines—we must open fresh windows and let in more light, so that we can see what these obstacles really are. It is in this work of discovery that it is hoped that this hospital will join hands with the university, and it is in this hope that some of the structures around you have been planned and provided.

Whenever and wherever the problems of higher medical education have been discussed within the last ten years, there has been speculation as to the probable course of the Johns Hopkins medical department, and the influence it would have upon the standard. . . . .

What is it then that the physicians want? Is it more physicians, more family practitioners, more surgeons, more specialists? They know very well that there is no danger that the supply will not be equal to the demand: when they become overburdened with practice, they do not at present find it difficult to obtain assistants; they have no fear lest the seventy or eighty medical schools of this country should fail to produce a sufficient number of medical practitioners to meet the wants of our increasing population; and they know also that the medical schools of Great Britain and Germany are sending to us quite as much of their product as we can conveniently dispose of. They hope that the Hopkins Medical School and Hospital will do two things. The first is, that it will demand of those who propose to become students, evidence that they have sound basis of preliminary education before they commence, and that its standard in this respect shall be little below that of the requirements for granting the degree of bachelor of arts in the university. It is hoped that the men thus selected will go through a carefully graded course of study, including actual work in properly fitted laboratories and that after this they will be brought into contact with the sick and thus obtain practical experience of the duties and responsibilities of the practitioner of medicine before they offer their services as such to the public. . . . .

In this country medical schools have either had no connection with universities, so called, or the connection has been slight and nominal, such as depends upon the formal conferring of degrees by the university. Here, however, through influence of the biological department, there are secured common interests and mutual influence, and it is hoped, therefore, that the necessary details of technological instruction will be arranged in accordance with and subordinate to the broad principles of scientific culture upon which this university is organized.

It is because it is believed that this will be the case that there is a widespread hope and expectation that these combined institutions will endeavor to produce investigators as well as practitioners, to give to the world men who cannot only sail by the old charts, but who can make new and better ones for the use of others. This can only be done where the professors and teachers are themselves seeking to increase knowledge, and doing this for the sake of the knowledge itself; and hence it is supposed that from this hospital will issue papers and reports giving accounts of advances in, and of new methods of acquiring knowledge, obtained in its wards and laboratories, and that thus all scientific men and all physicians shall share in the benefits of the work actually done within these walls. But however interesting and valuable this work may be in itself, it is secondary in importance to the future of science and medicine and to the world at large, in comparison with the production of trained investigators, full of enthusiasm, and imbued with the spirit of scientific research, who will spread the influence of such training far and wide. It is to young men thus fitted for the work that we look for the solution of some myriad problems which now confront the biologist and the physician.

Do I seem to ask too much: to be sanguine as to what human thought, and study and skill may accomplish; to forget that there is one event unto all; that the shadow of pain and death come on the wise man as on the fool? I have two answers. As surely as our improved methods of prevention and treatment, based on the advances in knowledge of the last fifty years, have already extended the duration of life in civilized countries nearly five years, have prolonged thousands of useful and productive lives, and have done away with indescribable agonies of the pre-anesthetic period, so surely we are on the verge of still greater advances, especially in the prevention of infectious and contagious disease, in the resources of surgery against deformities and morbid growths, and in the mitigation of suffering due to causes which cannot be wholly removed. But the second answer is more important and it is this: It is our duty to try to increase and diffuse knowledge according to the means and opportunities which we have, and not to rest idle because we cannot certainly foresee that we shall reap where we have strewn. "It is not incumbent on thee to finish the work, but thou must not therefore depart from it," says the Talmud, and "Of him to whom much is given much shall be required," says the Scripture.

These words of Dr. Billings show better than I could express it, the wisdom, the farseeing vision, the ideals and intellectual strength of the man. His influence upon hospital development and medical education cannot be over-estimated. How fortunate that at the very beginning and continuing for many years this institution had the benefit of his influence as a consultant and adviser to the trustees. These words are still full of meaning, and particularly to us officers, teachers and pupils in the institution for which he did so much, and who on this occasion pay tribute to his memory.

DR. JACOBS: The evening would not be complete unless we had Dr. Welch to summarize and to pay his tribute.

DR. WELCH spoke in part as follows: I regard it as one of the greatest influences of my life to have known Dr. Billings. I first became fairly well acquainted with him when I was a student in a pathological laboratory at Leipzig. Dr. Billings came there that winter and stayed several days. He came often to the laboratory, and delightful experiences were the evenings we spent with him in Auerbach's Keller talking about all sorts of things. He had already written about the Johns Hopkins

Hospital and was full of the future of this institution. I saw then one side of his activities—the most characteristic in a way—his extraordinary love of books and knowledge of medical literature.

The central work of Dr. Billings was of course the library of the surgeon-general's office, and the museum, enduring for all time. I question whether America has made any larger contribution to medicine than that made by Dr. Billings in building up and developing the surgeon-general's library and in the publication of the Index Catalogue and the Index Medicus. That in my judgment is our greatest contribution to medicine, and we owe it to this extraordinary man. Enough has perhaps been said as to the qualities of the man who organized and developed that great work. Dr. McCaw has rescued a little chapter in his life about which few knew anything—his experiences as an army surgeon. It is interesting to know how his experiences as an army surgeon influenced his subsequent work. The fact that he was an army surgeon brought him into the surgeon-general's office in Washington; and the opportunity offered there enabled him to develop this great library.

The other work which he did during the thirty odd years of his connection with that library was in a sense incidental to his work as librarian of the surgeon-general's office. Nevertheless this other work was highly significant. He was for a time our leading authority in hygiene in this country, at least in certain important branches. He was actively interested in the work of the American Public Health Association in its early days. I have no doubt that his interest in hygiene came from his experience in the war. In fact, his early publications indicate that; one being on hospitals and barracks; another, on army sanitation which appeared about 1870. Thus, you can trace from his army experience, the work of the library, and also his work in hygiene. The latter of course is not surprising, because an army surgeon should be interested in hygiene and sanitation, as the natural result of his professional interest. Not so, however, his interest in bibliography and the building up of a library, an extraordinary and absolutely unique work for an army surgeon, in a young country like ours. When asked what America had contributed to medicine, you would not expect to reply the building of a library and preparation of an Index Catalogue. You might expect it in a country like France or Great Britain. Nevertheless, that is our contribution, and as Dr. Thayer has said, that library has had a marked influence upon the medical outlook in this country. Greater justice is done here to the discoverer in medicine than elsewhere, and a much more careful effort is made to see that a full record is kept of what has already been done, so that historical justice may be given to previous work; so the very characteristics of our medical literature are in a sense a tribute to Dr. Billings' work.

His work as a hygienist was important. He was the greatest authority on everything relating to sanitation, hospital construction, heating and ventilation. Then he was the greatest vital statistician this country has produced. His connection with the tenth and eleventh census was of the first significance. The character of the data collected for them was due to the thought which he gave to the matter, and his analysis of the vital statistics of cities in connection with the eleventh census was a most important piece of work. Dr. Billings was the Cartwright lecturer at the College of Physicians and Surgeons in New York in the late '80's and his lectures were devoted to this subject. It is not surprising when he retired from the army, that he should have been selected to be professor of hygiene in the newly founded laboratory of hygiene at the University of Pennsylvania.

Dr. Norton I think is under misapprehension as to his fame. His was our most famous name, so far as European reputation is concerned, with the possible exception of Dr. Weir Mitchell, during the decades between 1870-1890. He had the widest acquaintance and was the most highly esteemed of American physicians. He was the one whose presence was desired to represent American medicine on special occasions. He was the recipient of honorary degrees from Dublin, Edinburgh and Oxford. His was a great name and a great influence in the world of medicine.

His influence was also great upon American medicine. I believe he had the making of a great surgeon, but he was withdrawn from active practice. When you consider that he was a librarian, a bibliographer, a writer on hygiene and a writer on sanitation, it is remarkable what his influence was. Of all the men I have ever known, he was about the wisest. He was a man whose judgment you sought on any difficult subject, and you pinned your faith to him more than to any man of your acquaintance. He was wisest because he was under no illusions. He got at the heart and essence of things. He was an eminently sane man, who knew what it was best to do under the circumstances, and what it was practicable to do. This quality was associated with a wide vision and high ideals. Some of his utterances were much resented by the average physician—the somewhat chauvinistic American doctor. Read two of his addresses which made a great stir at the time. One is the centennial address at Philadelphia in 1876 on American medicine. And above all, read the address which was resented by some members of our profession, "Medicine in America," given before the British Medical Association in 1886. Somewhat facetiously, but fairly seriously, he discussed the subject of malaria, and declared that certain portions of this country had been rather sterile in the matter of investigation and prevention. He was half-jocose, but at the same time he candidly stated how meagre had been our contributions. This view was the opposite of the usual Fourth of July, spread-eagle style of address, but it was well to have it said; and he said it well! At the same time I would not convey the impression that he was not a patriotic American. There were none more so, but he put things exactly as they were. He was a lover of truth, and he would spare nothing in order to reach the truth and kernel of a matter.

He was not an educator, but of course his influence on American education was considerable. As has already been pointed out, what this hospital is to-day is mainly the thought of Dr. Billings. He conceived of it as a place not only for the

care of patients, but for teaching and for investigation—the three great functions of a hospital. All three were conceived of as essential parts of its work. He was here as the adviser of the trustees of the hospital from about 1876, I think, or 1877, until the time when the hospital opened. They would have been only too glad to have him become the superintendent of the hospital. It would have been a pity in a sense to have him give up his great work in Washington. Dr. Billings gave several courses of lectures on medical education at the university, and later at the hospital.

The medical school was famous before it existed. There was a great deal of discussion as to what the school was going to be, and no one had more influence than Dr. Billings. There was a little medical faculty here even before I came in 1884. The hospital opened in 1889 and the medical school in 1893, but the records of our medical faculty begin before the opening of the hospital and the medical school. There was a little group, consisting of President Gilman, Ira Remsen, professor of chemistry; Newell Martin, professor of biology, and Dr. Billings, and the data collected by them are extremely interesting. When we planned to open the medical school, our most perplexing matter was the question of requirements for the admission of students—elaborate requirements which represented such a step beyond what existed at that time! Not even a high school requirement generally existed then. We were alarmed at the prospect and had no formal opening of the medical school. We feared that nobody would come, because we felt that we ourselves could not have gotten in and we did not know whether any such students as we desired existed at that time. Dr. Billings was in our councils, and one of his contributions was a little publication privately circulated, in which he gave the requirements for the doctor's degree in all the leading universities in the world. You may imagine how helpful that was when we were endeavoring to determine our requirements for admission.

Nothing has been said about the great work of his later years as the librarian of the great Public Library in New York. There he supervised the erection of its great building and the consolidation of the three great foundations—the Astor, the Lennox, and the Tilden. He organized the library which in New York they believe to be his greatest work. At the recent memorial meeting in the Public Library—a most interesting meeting—Andrew Carnegie, Dr. Weir Mitchell, Dr. Osler, John L. Cadwallader and others spoke, and emphasis was laid upon it as his greatest and most important work. You can see how great the man was when just at the end I can only touch upon what many believe to be his greatest work. I do not so believe it to be. I think his greatest work was the building up of the library in Washington and the publication of the Index Medicus and the Index Catalogue. Dr. Osler says the fame of bibliographers lives. Haller will probably be known longer as a bibliographer than as a contributor to knowledge. Gessler will probably be known longest in a similar way. Dr. Billings was the greatest bibliographer in the history of medicine.

DR. JACOBS: These are our tributes to Dr. Billings.

NOTES ON NEW BOOKS.

Meningococcus Meningitis. By HENRY HEIMAN, M. D., and SAMUEL FELDSTEIN, M. D. Introduction by HENRY KOPLIK, M. D. Illustrated. $2.50. (*Philadelphia and London: J. B. Lippincott Company, 1913.*)

In this monograph of 307 pages, the present knowledge of the meningococcus infections of the meninges is presented. Free use of the clinical material of other workers has been made together with that which the authors themselves have had. The various aspects—bacteriology, epidemiology, symptomatology, etc.—of this disease are considered in a thorough manner. The completed bibliography adds to the value of the work and most of the illustrations are good. The book should prove of usefulness, especially to physicians engaged in clinical work.

A Reference Handbook of the Medical Sciences. Edited by THOMAS LATHROP STEDMAN, M. D. Vol. III. Illustrated. Embossed. $7. (*New York: William Wood & Co., 1914.*)

With one exception all the contributors to this volume are Americans, the lonely stranger is a Canadian; and the list of names is representative of the best men in the profession throughout the United States. This broad selection of authors gives this handbook authority which would be lacking were it a more local production. It contains a great deal of information not readily found except in a large library, so that it at once becomes a most useful book for almost any physician, if he is willing to wait for all eight volumes. It is a thankless and a most exhaustive task to edit such a work, and one for which few are so well fitted as Dr. Stedman; he is to be congratulated on getting out these large volumes as rapidly as he does, and in so successfully keeping such a high standard throughout. This handbook can be referred to with the assurance of finding accurate, helpful and reliable information.

Where the lapse of time between the appearance of the volumes is considerable it would seem better to give some definition to every term embodied, and not say "see ——," another reference which may not be found until the last volume appears. There are articles in this volume, as for instance, on the "ear," which, it seems to us, could be much shorter. In this article one finds more than in many small works on this subject. One would not naturally turn to such a handbook for information as to how to perform certain operations, so why should these be given in detail? The choice of illustrations might be discussed at length—why some are selected and many others omitted? The reproductions are not remarkable and many are poor. The lists of references appended to papers vary in length and form; there should be more uniformity practiced in their arrangement and abbreviations.

The Unexpurgated Case Against Woman's Suffrage. By SIR ALMROTH E. WRIGHT. $1. (*New York: Paul B. Hoeber, 1913.*)

The author has not added to his distinction as a scientific investigator by this work. The fanatic opponents of suffrage have as little reason on their side as the fanatic supporters, and Sir Almroth Wright's plea against giving women the right to vote carries very little conviction and weight with it. The publication of this essay is to be regretted from almost every point of view.

THE QUARTER CENTENNIAL ANNIVERSARY OF THE OPENING OF THE JOHNS HOPKINS HOSPITAL AND THE TWENTY-FIRST ANNIVERSARY OF THE OPENING OF THE MEDICAL SCHOOL

Will be observed by appropriate exercises beginning October 5, 1914, and continuing during the week.

The exercises upon Monday, October 5, 9.30 a. m. to 12 m., are to be especially arranged for by the Training School for Nurses and will be announced later.

Upon Monday at 3.30 p. m., the formal opening meeting will be held at the Lyric, with addresses by Dr. W. H. Welch, Sir William Osler, Miss M. Adelaide Nutting and Dr. H. M. Hurd.

In the evening there will be dinners of the former Medical Officers of the Hospital, and of the Alumnæ of the Training School for Nurses.

Upon Tuesday, October 6, 9.30 a. m. until 12 m., papers upon medicine by former members of the staff will be presented in the Medical Amphitheatre. Papers or demonstrations of methods of study of Psychiatry at the Henry Phipps' Clinic from 10 a. m. to 12 m. Gynecological operations in the Surgical Amphitheatre from 10 a. m. until 1 p. m. A Clinic by Sir William Osler at 12 m.

Luncheon at the Hospital from 1 to 2.30 p. m.

From 2.30 to 3.30 p. m. Clinic in the Harriet Lane Home by Dr. John Howland. At 3.30 p. m., a dedication of the Hewetson Medallion.

A demonstration of Nurses' work in the Medical Amphitheatre from 4 to 5 p. m.

From 4.30 to 5.30 p. m., a lecture on the Herter Foundation by Dr. Thomas Lewis of London.

In the evening a Dinner of the Alumni of the Medical School.

Wednesday, October 7, from 9.30 a. m. to 1 p. m., Surgical Operations in the Surgical Amphitheatre.

From 11 a. m. to 1 p. m. Visits to Medical Laboratories.

1 p. m., Luncheon.

At 3.30 p. m., Dedication of the James Buchanan Brady Urological Clinic, with addresses by Dr. Winford Smith, President Goodnow of The Johns Hopkins University, Dr. H. H. Young, and others.

A Garden Party upon the lawn of the Hospital at 5 p. m.

In the evening a Subscription Dinner to Mr. James Buchanan Brady. Also Class Dinners.

Thursday, October 8, 9.30 a. m. to 1 p. m., Papers in Pathology in the Medical Amphitheatre.

Also Papers or Addresses upon Obstetrical Topics in the Surgical Lecture Room, 10 a. m. to 12 m. Operations in Urological Surgery in the Surgical Amphitheatre, 10 a. m. to 12 m.

1 to 2.30 p. m., Luncheon.

4.30 p. m., Second Herter Lecture by Dr. Lewis.

In the Evening, Class Dinners.

Friday, October 9, 4.30 p. m., Third Herter Lecture by Dr. Lewis.

More detailed programmes will be published later.

During the Anniversary Week laboratory demonstrations will be given in the laboratories of the Medical School as follows:

In the Anatomical Laboratory, By Prof. Mall and the Anatomical Staff.

In the Physiological Laboratory, By Prof. Howell and the Physiological Staff.

In the Pharmacological Laboratory, By Prof. Abell and the Pharmacological Staff.

The exact dates and hours of such demonstrations will be announced in the final program.

PROGRAMME FOR THE CELEBRATION OF THE TWENTY-FIFTH ANNIVERSARY OF THE OPENING OF THE JOHNS HOPKINS HOSPITAL

MONDAY October 5	TUESDAY October 6	WEDNESDAY October 7	THURSDAY October 8
9.30–12 Nurses' Training School	9.30–12 Medicine (Medical Amphitheatre) Psychiatry 10–1 Gynecology (Surgical Amphitheatre) 12 Clinic Sir William Osler	9.30–1 Surgery (Surgical Amphitheatre) 11–1 Medical Laboratories	Pathology (Medical Amphitheatre) Obstetrics (Surgical Lecture Room) 10–12 Urological Surgery (Surgical Amphitheatre)
	1–2.30 Luncheon	Luncheon	Luncheon
2.30 Opening Meeting (The Lyric) Addresses: Dr. W. H. Welch presiding Sir Wm. Osler Dr. H. M. Hurd Miss M. A. Nutting	2.30 Pediatric Wards Dr. Howland 3.30 Dedication Hewetson Medallion 4.30 Herter Lecture	3.30 Dedication of the J. B. Brady Urological Clinic Dr. W. H. Smith presiding Pres. F. J. Goodnow Dr. H. H. Young and other speakers 5 Garden Party (The Lawn)	4.30 Herter Lecture
Dinners Johns Hopkins Hospital Alumni Nurses	Dinner Alumni of Medical School	Dinner to Mr. J. B. Brady, Donor of the new Urological Clinic Class Dinners	Class Dinners

THE HERTER LECTURES FOR 1914.

The Herter Lectures will be given in connection with the Quarter Centennial Anniversary of the Opening of The Johns Hospital and the Twenty-first Anniversary of the Opening of the Medical Department of The Johns Hopkins University, upon Tuesday, Thursday and Friday, October 6, 8 and 9, 1914, at the Physiological Lecture Room, Monument and Washington Streets, at 4.30 p. m., by Thomas Lewis, M. D., University College, London, England.

Dr. Thomas Lewis in charge of the heart station at University College, and Editor of *Heart* has done important work in the study of cardiac conditions, and will present three lectures on the scientific study of the heart and its bearing on clinical medicine. He is the first clinical investigator who has filled the position of Herter Lecturer. The titles of his lectures will be announced later.

The Johns Hopkins Hospital Bulletins are issued monthly. They are printed by the LORD BALTIMORE PRESS, Baltimore. Subscriptions, $2.00 a year (foreign postage, 50 cents), may be addressed to the publishers, THE JOHNS HOPKINS PRESS, BALTIMORE; single copies will be sent by mail for twenty-five cents each. Single copies may also be procured from the BALTIMORE NEWS CO., Baltimore.